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Behavioral Incapacitation from a High Dose of Ionizing Radiation

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13. ABSTRACT *(Maximum 200 words)*
This report presents the methods and the results of an analysis of incapacitation data of monkeys irradiated at the Armed Forces Radiobiology Research Institute between 1968 and 1982.

One hundred and ninety-three animals were trained to perform a cognitive task and 39 were trained to perform a locomotion task. The cognitive tested animals were subdivided into those irradiated at a neutron/gamma ratio of 3:1 and/or 4:10. All locomotion tested animals were irradiated at a neutron/gamma ration of 3:1.

Probits were fit to the minute-by-minute performance data for each group which were then smoothed across time using a unique Monte Carlo method. The results of these analyses present percent (proportion) incapacitated versus time graphs for a wide range of radiation doses for the cognitive and for the locomotion tasks. Graphs of the 25, 50 and 75% isoperformance curves are also provided.

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SUMMARY

In addition to the signs and symptoms of the prodromal syndrome of acute radiation sickness, early transient incapacitation (ETI) has been observed in man. Animal data are used to describe this incapacitation because large high-dose-rate exposures to man have occurred too infrequently to permit the quantification of transient incapacitation in terms of dose and time after exposure.

The monkey was chosen as the model for incapacitation because (a) the intelligence and dexterity of the monkey permit testing on tasks that model human behavior, (b) following exposure to doses in the same order of magnitude, acute radiation symptoms are similar, and (c) the sequela of incapacitation is similar for both species.

Current military requirements are such that performance degradation must be clearly defined and described over a wide range of doses up to 18000 cGy free-in-air. To simulate battlefield environments, the dose must be from rapidly delivered mixed fission-spectrum fields over a wide range of neutron-to-gamma ratios, and referenced at the midhead point.

Animal performance studies have shown that incapacitation is qualitatively the same over a wide range of behavioral tasks, but varies quantitatively as a function of the physical demand of the task. Therefore, separate tasks were chosen to model physical and cognitive performance for this study. The cognitive task was a sequential visual discrimination task (VDT) performed by chaired monkeys; the physical task tested locomotor activity in a physical activity wheel (PAW). Shock avoidance tasks were used because of interference between the radiation-induced nausea, vomiting, and anorexia and the food reinforcement. Performance was stabilized before exposure to radiation.

Each subject was exposed to a single 10-msec (full width at half maximum) pulsed dose of mixed neutron-gamma radiation from the AFRRI TRIGA reactor. The unmoderated field produces a neutron-to-gamma (N/g) ratio of 4:10 at 125 cm from the core centerline.

To vary the N/g ratio, the field was modified with a 5 cm lead shield which produced a 3:1 field 90 cm from the core centerline. The subjects were irradiated with their backs to the core. Cognitive-task subjects were in Plexiglas chairs, and physical task subjects were in a Plexiglas box.

Extensive phantom dosimetry, backed up by theoretical (Monte Carlo and discrete ordinate) calculations, was used to provide estimates of the midhead dose for each subject. Dosimetry measurements were made for each exposure with ionization chambers and sulphur foils. The midhead location was used because (a) behavior was the variable of interest, and it was originally thought that the central nervous system was the site of injury, and (b) most battlefield doses are calculated at the height of the midhead. The assumption is that an effect (incapacitation) resulting from a given dose delivered to the midhead of a monkey would be the same if the same dose were delivered to the midhead of a man. Extensive state-of-the-art Monte Carlo calculation of doses expected from actual stockpile weapons (both free-in-air and in theoretical human tissue models) have been made in order to translate the midhead monkey doses, estimated in the reactor, to free-in-air kerma battlefield doses.

The present analysis is based on data from (a) 141 VDT animals exposed to doses ranging from 1050 to 17570 cGy FIA in a N/g = 4:10 field, (b) 52 VDT animals exposed to doses ranging from 1825 to 5820 cGy FIA in a N/g = 3:1 field, and (c) 39 PAW animals exposed to doses ranging from 1600 to 6200 cGy FIA in a N/g = 3:1

field. Minute-by-minute postirradiation performance histories were available for the first 2 hours for the VDT animals, for the first 6 hours for the PAW animals, and at regular intervals thereafter for all animals.

The three groups of test results were treated similarly. A probit function was fitted to the data separately for each group at each minute, using the full range of doses and the associated ones or zeros that indicated whether the animal was capable or incapable of performing the task. The probit function permitted estimation of the percent incapacitated at any dose within the range tested; it provided estimates of confidence for the percent incapacitated estimates, and provided smoothing across the doses. The Box-Cox transformation was used to linearize the dose-response function over the range of doses. A method of decomposition of the time-versus-incapacitation curves was developed to recreate individual time histories. The primary function of this method is to feed individual time histories into combat simulation models, but it also provides an excellent smoothing-through-time technique that closely follows the data while smoothing out the small fluctuations due to chance.

The end result is a smoothed family of curves for each data set (VDT at 4:10, VDT at 3:1, and PAW at 3:1), showing the percent incapacitated versus time to 10,000 minutes (7 days) after irradiation at doses from 1000 to 15000 cGy FIA. The final curves show that (a) percent incapacitated is a monotonic increasing function of dose; that is, a higher dose produces at least as many incapacitations as a lower dose; (b) a peak in percent incapacitated occurs 5 to 15 minutes after irradiation; (c) this peak is followed by one or more periods of recovery; (d) the N/g = 4:10 animals reach permanent complete incapacitation (PCI) later than the N/g = 3:1 animals; (e) PAW animals have a distinct secondary recovery period at about 1 hour; and (f) the

VDT animals in the N/g = 3:1 field reach PCI earlier than the PAW animals in the N/g = 3:1 field.

The information contained in these families of curves provides estimates of the percentage of individuals incapable of performing their tasks performing their tasks due to behavioral incapacitation at a given time postexposure. As such, these curves can be used to define the times after irradiation when individuals would be incapacitated for various combat tasks. These data, combined with the individual profiles of performance decrement due to radiation sickness, can be used to provide a complete estimate of post-irradiation performance for each combat task.

PREFACE

This report presents a unique and highly original analysis encompassing all of the existing data on high-dose-rate irradiated monkeys performing a visual discrimination or a physical activity wheel task.

The research was done at the Armed Forces Radiobiology Research Institute (AFRRI) by a series of research psychologists and physiologists between 1968 and 1982.

All of the authors of this report were employed at the AFRRI in 1981 when the research was completed. R. W. Young and C. G. Franz were investigators in the Behavioral Science Department and conducted many of the experiments described in this report. S. G. Levin and W. E. Jackson were biostatisticians in the Statistics and Computer Science Department. Dr. Young has subsequently moved to the RARP division of the Defense Nuclear Agency and Mr. Levin is now employed by Technico Southwest Inc.

The analysis described in this report was undertaken to satisfy the needs of the US Army Nuclear and Chemical Agency in developing personnel risk and casualty criteria.

Acknowledgments:

Figure 2-1 is taken from deHaan (1968) and Figure 2-2 is taken from Curran (1974).

Figures 4-4 and 4-5 are taken from Anno (1984).

The other figures in this report were drawn by Kathy Summers from computer generated figures calculated by William Jackson. The manuscript was typed by Dawn Autrey and edited by Hoover Ogata.

CONVERSION TABLE

Conversion factors for U.S. Customary to metric (SI) units of measurement.

MULTIPLY → / TO GET ←	BY → / BY ←	TO GET → / DIVIDE ←
angstrom	1.000 000 X E -10	meters (m)
atmosphere (normal)	1.013 25 X E +2	kilo pascal (kPa)
bar	1.000 000 X E +2	kilo pascal (kPa)
barn	1.000 000 X E -28	meter^2 (m^2)
British thermal unit (thermochemical)	1.054 350 X E +3	joule (J)
calorie (thermochemical)	4.184 000	joule (J)
cal (thermochemical/cm^2)	4.184 000 X E -2	mega joule/m^2 (MJ/m^2)
curie	3.700 000 X E +1	*giga becquerel (GBq)
degree (angle)	1.745 329 X E -2	radian (rad)
degree Fahrenheit	$t_k = (t°f + 459.67)/1.8$	degree kelvin (K)
electron volt	1.602 19 X E -19	joule (J)
erg	1.000 000 X E -7	joule (J)
erg/second	1.000 000 X E -7	watt (W)
foot	3.048 000 X E -1	meter (m)
foot-pound-force	1.355 818	joule (J)
gallon (U.S. liquid)	3.785 412 X E -3	meter^3 (m^3)
inch	2.540 000 X E -2	meter (m)
jerk	1.000 000 X E +9	joule (J)
joule/kilogram (J/kg) radiation dose absorbed	1.000 000	Gray (Gy)
kilotons	4.183	terajoules
kip (1000 lbf)	4.448 222 X E +3	newton (N)
kip/inch^2 (ksi)	6.894 757 X E +3	kilo pascal (kPa)
ktap	1.000 000 X E +2	newton-second/m^2 ($N-s/m^2$)
micron	1.000 000 X E -6	meter (m)
mil	2.540 000 X E -5	meter (m)
mile (international)	1.609 344 X E +3	meter (m)
ounce	2.834 952 X E -2	kilogram (kg)
pound-force (lbs avoirdupois)	4 448 222	newton (N)
pound-force inch	1.129 848 X E -1	newton-meter (N·m)
pound-force/inch	1.751 268 X E +2	newton/meter (N/m)
pound-force/foot^2	4.788 026 X E -2	kilo pascal (kPa)
pound-force/inch^2 (psi)	6.894 757	kilo pascal (kPa)
pound-mass (lbm avoirdupois)	4.535 924 X E -1	kilogram (kg)
pound-mass-foot^2 (moment of inertia)	4.214 011 X E -2	kilogram-meter^2 ($kg·m^2$)
pound-mass/foot^3	1.601 846 X E +1	kilogram/meter^3 (kg/m^3)
rad (radiation dose absorbed)	1.000 000 X E -2	**Gray (Gy)
roentgen	2.579 760 X E -4	coulomb/kilogram (C/kg)
shake	1.000 000 X E -8	second (s)
slug	1.459 390 X E +1	kilogram (kg)
torr (mm Hg, 0° C)	1.333 22 X E -1	kilo pascal (kPa)

*The becquerel (Bq) is the SI unit of radioactivity; 1 Bq = 1 event/s.
**The Gray (GY) is the SI unit of absorbed radiation.

TABLE OF CONTENTS

TABLE OF CONTENTS

FIGURES

FIGURES (continued)

FIGURES (continued)

TABLES

SECTION 1
INTRODUCTION

Combat ineffectiveness after exposure to nuclear radiation can be caused by early transient incapacitation (ETI), episodes in which the subject becomes totally incapable of performing, and performance degradation due to radiation sickness. Although performance degradation for humans due to radiation sickness as a function of intermediate dose, doses 75-4500 cGy, has been quantified by the research efforts of the DNA Intermediate Dose Program (IDP) (Anno, 1989), the frequency and duration of episodes of early transient incapacitation in humans following high-dose-rate exposures and the percentage of persons so affected has not been defined. There are not sufficient data on humans exposed to superlethal high-dose-rate irradiation to predict such figures. While many accidental human irradiations have occurred, only two are high-dose-rate, mixed neutron-gamma fission spectra exposures of the type expected in tactical nuclear warfare. In one case (Shipman, 1961), the man involved was able to turn off his equipment, run from the building and speak to his colleagues after being exposed; however, within minutes he became incoherent, ataxic and incapacitated. One hour and 40 minutes after exposure, the victim was coherent and sufficiently improved to be transferred from the hospital emergency room to a regular treatment room, despite the continued grave clinical picture. The dose received by this man was calculated to be 4500 cGy averaged over the whole body, with a dose of 10000 to 12000 cGy to the front of the head.

Lacking data on the ETI response of humans to superlethal high-dose-rate neutron/gamma irradiation, it becomes necessary to rely on data on the response of animals to predict what the response of humans would be, so that the performance of military personnel

and units so exposed can be reliably predicted. The behavioral response to total-body irradiation has been most studied in the dog, rat, miniature pig and monkey. The dog vomits but does not exhibit a transient incapacitation in response to radiation (Chaput, 1972). The rat and pig exhibit transient incapacitation after irradiation (Casarett, 1973; Chaput, 1970) but with major differences from the response observed in man. The rat does not vomit (Casarett, 1973), and the radiation dose required to incapacitate the rat is approximately an order of magnitude higher than for other animals. The onset of incapacitation in the miniature pig occurs almost immediately after irradiation (Chaput, 1970), whereas in man the onset is delayed a few minutes (Allen, 1960). Also, incapacitation in the pig is accompanied by opisthotonoid convulsions (Chaput, 1970); in man it is not (Allen, 1960).

Prediction of human response from animal data requires some confidence in the validity of the assumption that the responses are the same. Several factors suggest that the monkey is the best animal model for predicting incapacitation in man. First, the monkey is more like man in behavioral repertoire, intelligence, nervous system development, dexterity and phylogenetic development than any other animal in which radiation effects have been studied. Second, the sequela of acute radiation sickness in response to doses of the same order of magnitude is the same for monkey and man. Third, both monkey and man have been observed to exhibit ETI in the same time frame with the same sequela after irradiation.

The basic assumption in relating incapacitation in the monkey to that in man has been (Warshawski, 1976) that a given dose delivered to the midhead of a monkey and man would have the same effect on both. The midhead location is used because the response is behavioral, and the presumed site of susceptibility is the

central nervous system. Furthermore, the Army uses the midhead height to calculate the free-in-air battlefield kerma.

The effects of total-body irradiation on the monkey has been systematically studied using a number of behavioral measures, and sufficient data have been collected to permit a determination of the ETI response. Previous analyses of these data have been made, but the development of new computers and analytic tools has made it possible to make a more detailed and usable estimate of ETI and its effect on the probable performance of military individuals and units in tactical nuclear combat, and the results are more readily adaptable to combat models. The U.S. Army Nuclear and Chemical Agency uses "Immediate Transient Incapacitation" (ITI) in place of ETI because it is more relevant to military tasks.

SECTION 2
EXPERIMENTAL SETUP

2.1 GENERAL.

In order to characterize incapacitation as a function of dose and time after irradiation, a series of studies was conducted by the Behavioral Science Department of the Armed Forces Radiobiology Research Institute (AFRRI). Those studies evaluated early transient incapacitation (ETI) following exposure in two reactor-generated mixed neutron-gamma radiation fields using rhesus monkeys trained to perform two different behavioral tasks. A visual discrimination task (VDT) was used as a model for performance of a physically undemanding task, and a physical activity wheel task (PAW) was used to evaluate performance of a physically demanding task. Shock avoidance was the incentive chosen in this study since radiation exposure can produce nausea, vomiting and anorexia, which would significantly interfere with a food incentive and thus potentially confound the interpretation of any radiation effect on behavior. All of the animals were given total-body exposures to a mixed neutron-gamma fission-spectrum radiation field having a neutron-to-gamma ratio of either 4:10 or 3:1.

2.2 VISUAL DISCRIMINATION TASK.

2.2.1 Subjects.

The subjects of the experiment were 141 juvenile, male rhesus monkeys (Macaca mulatta). Their mean age was 3.4 years (range of 2.5 to 4.5 yr) with a mean weight of 3.4 kilograms (range of 2.4 to 5.3 kilograms). All subjects were trained and irradiated in standard Plexiglas monkey chairs, in keeping with the guidelines for laboratory animals enunciated in the National Academy of

Sciences--National Research Council "Guide for Laboratory Animal Facilities and Care". The animals had food and water available ad libitum.

2.2.2 Behavioral Testing.

Each subject was trained to perform a discrete-trial shock-avoidance visual discrimination task. The monkey was required to discriminate between a circle and a square presented on two back-lit Foringer response keys using Institute of Electrical Engineers (IEE) stimulus display units. The square was always the correct response, but the relative positions of the circle and the square were switched randomly from trial to trial. Each paired presentation of the circle and square was counted as a behavioral trial. Trials were presented at 10-second intervals, with each trial initiated by the simultaneous illumination of the two stimulus-response keys and a 25-watt house light in the animal's test cubicle. The subject was given 5 seconds to press the correct key. If the subject failed to press either key within 5 seconds, the trial was scored as an omission. If the subject pressed the wrong key within 5 seconds, the trial was scored as an incorrect response. Pressing the correct key within 5 seconds extinguished the stimulus display, and the cubical light. After either an incorrect response or an omission, the following sequence ensued: the stimulus keys were extinguished, but the cubical light remained on, and a Sonolert tone came on for 1 second; the tone served as a pre-aversive stimulus. After 1 second, the tone stopped, and a 1.0-second 5-milliampere shock was delivered to the subject from a Foringer shocker between two skin-surface electrodes attached to the small of the back and the tail. Each trial was scored as either correct, incorrect, or omission, and the time to respond (response latency) of each trial was recorded. The sequencing of the behavioral tasks and the recording of the response data were controlled by a portable rack of BRS-Foringer relay logic.

Behavioral data were recorded in real time, together with a continuous time code on a Hewlett-Packard analog tape recorder. Taped data were subsequently transferred to a PDP 11-45 computer for digitizing and analysis.

Subjects were trained and tested in a sound-attenuated isolation cubical (Figure 2-1) having a one-way window for visual observation, and a closed circuit television camera recorded the animal's performance.

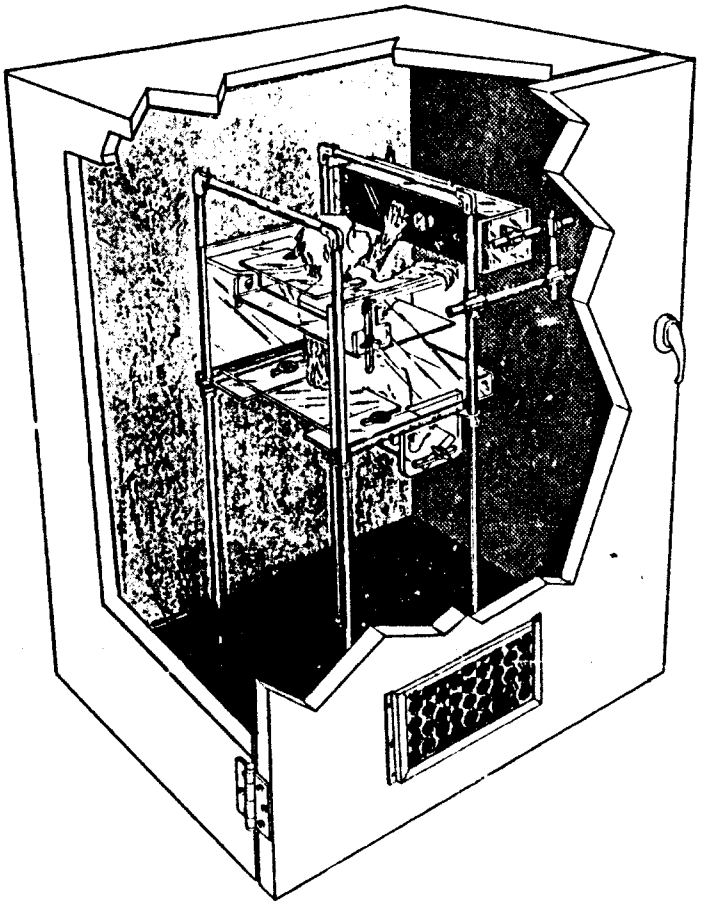

Figure 2-1. Visual discrimination testing apparatus with chaired monkey facing response console.

2.2.3 Procedure.

After learning the visual discrimination task, all subjects were given sufficient practice trials to allow performance to stabilize. Once a stable performance level of at least 95 percent correct responses was reached, the animal was given a pre-irradiation baseline performance test. This test consisted of 820 trials in the following sequence: (a) a 16-minute 100-trial pretest, (b) a 14-minute break, (c) an uninterrupted 2-hour 720-trial session. This entire testing sequence covering 2.5 hours was completed in the AFRRI TRIGA reactor radiation exposure room. After the testing, each subject was returned to the laboratory for further testing and observation. The baseline test was used to confirm the subject's performance stability, and served as a same-subject control for postirradiation comparison. Two days after the baseline test, the animals were again taken individually to the radiation exposure room. They were given the 16-minute 100-trial pretest and a 14-minute break, were irradiated, and were then given the uninterrupted 2-hour test session. Food was withheld for 18 hours before radiation exposure in order to control the interaction of food ingestion and postirradiation emesis.

2.2.4 Data Collection.

The purpose of these studies was to determine the frequency and duration of early transient incapacitation, emesis, and the time to death resulting from high doses of total-body irradiation. Electronic instruments recorded the responses (correct, incorrect or omission) and the time from stimulus to response. Review of the video recording provided time to and duration of emesis episodes and time to permanent complete incapacitation (PCI) or death. The following variables were then calculated from the basic data:

* Number of correct responses, incorrect responses, and omissions
* Time to respond

* Number, duration and time of incapacitations
* Number, duration and time of emesis episodes

2.3 PHYSICAL ACTIVITY WHEEL.

2.3.1 Subjects.

Thirty-nine naive, male rhesus monkeys (Macaca mulatta) were used in this study. They were housed individually in stainless steel cages in a restricted-access primate colony with a cycle of 12 hours light and 12 hours dark running from 0600 to 1800 hours. Their mean age was 44.9 ± 1.66 months (range of 26 to 72 months), and their mean weight was 5.45 ± 1.18 kilograms (range of 3.0 to 7.1 kilograms). Subjects were maintained on Purina monkey chow and fruit; water was available ad libitum in both cages and training apparatus. Subjects were fasted for 14 hours before irradiation.

2.3.2 Behavioral Testing.

Training and testing were done in a nonmotorized physical activity wheel consisting of a circular treadmill (24 inches wide, 4 feet in diameter) that rotated freely on four ball bearings between two 5/8-inch Plexiglas walls (Figure 2-2). The wheel was constructed of 1/2-inch Plexiglas and 3/8-inch-diameter aluminum rods (Germas, 1969). A 1/2-pound pull on the tangent was sufficient to initiate wheel rotation.

A microswitch was tripped to indicate a revolution, and a tachometer indicated the speed in mph. The 120 aluminum bars on the periphery of the wheel were connected to a shock generator, and served as both running surface and a shock grid. Shock intensity could be adjusted between 0 and 10 milliamperes. A motor-driven brake was used to stop the wheel for rest periods and to reduce excessive speed. One of the support walls contained

a small door that could be opened by remote control. A Plexiglas restraint box used to transport the subjects was mounted against the door; when the door was opened, it allowed subjects to enter the wheel. A shock grid was placed on the floor of the box to prevent subjects from reentering.

Two displays for presentation of color visual cues were mounted on the support wall opposite the door. The auditory stimulus consisted of a high-frequency tone interrupted by a pulse generator to vary the beats per minute. The tone stimulus was generated by a speaker (2 inches, 3.2 ohms) located above the lights.

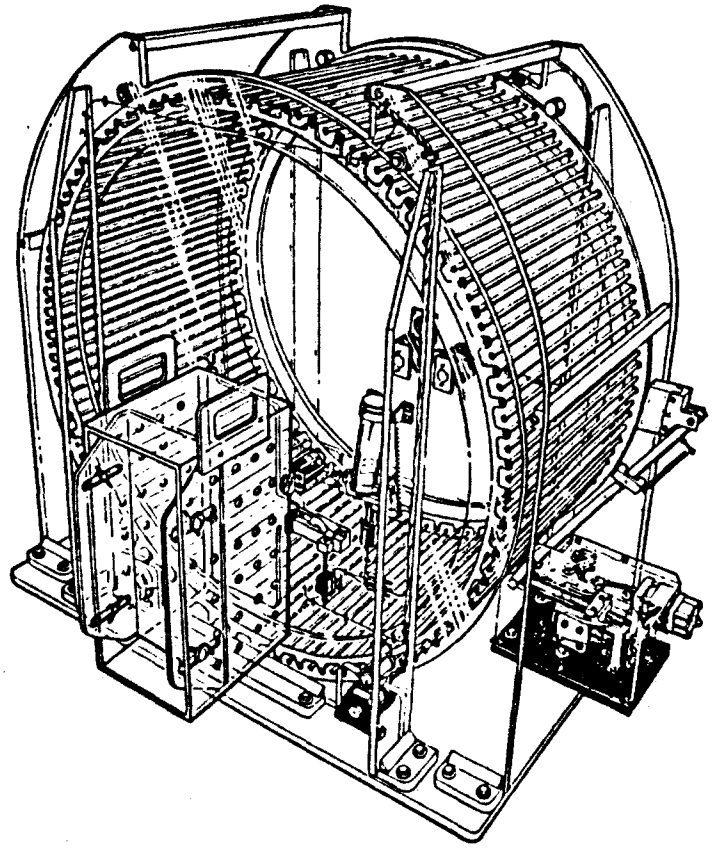

Figure 2-2. Physical activity wheel apparatus.

Performance was guided by a shock-motivated, free-operant reinforcement schedule (Curran, 1974) with visual and auditory cues (Table 2-1). Subjects could indefinitely avoid shock by

rotating the wheel at or above 1 mph. If the speed exceeded 5 mph, the brake automatically increased the drag on the wheel until the speed dropped below 5 mph, because pilot studies showed that subjects could injure themselves at speeds in excess of 5 mph. During rest periods when the brake held the wheel in a fixed position, no visual or auditory cues were presented. However, 30 seconds before the end of the rest period, the brake was gradually released, and a tone and light were turned on to indicate the beginning of a 10-minute work period. The shock was disabled until the brake was completely off.

2.3.3 Procedure.

Subjects were trained for at least 9 weeks (2 hours per day; 5 days per week) until the 10 minute work/5 minute rest cycles could be maintained in a six-hour continuous test. Performance was measured as the mean running speed for each 10-minute work period. When running speed in the 10-minute periods did not vary more than ± 20% for the 6 hours, training was complete and the subjects were sham-irradiated. Subjects were tested in the wheel for 2 hours in the radiation exposure room and four hours in the training room. The normal training schedule was resumed for 5-days after sham-irradiation.

Table 2-1. Auditory, Visual and Shock Task-Control Parameters

	Speed mph	Tone (BPM)	Lights	Shock
Shock zone	0-1	90	green	0.4-s pulse every 1.3 s[a]
Shock avoidance danger zone	1-3	90	green	none
Shock avoidance safe zone	3-5	60	white	none
Overspeed zone	>5	30	red	none[b]

[a] 0.4-s pulse once every minute during incapacitation
[b] Brake moves to "on" position

On the day of irradiation, the subjects were transported to the exposure room and given a 10-minute pretest. If the pretest running speed was ± 20% of that achieved during the first 10 minutes of the sham-irradiation, the subjects were placed in the restraint box and irradiated. If the subject failed the pretest, training was resumed for an additional 8 days before a second sham-irradiation.

After irradiation the subject was released from the box into the physical activity wheel within 45 seconds, and testing began. The first day of postirradiation, testing was identical to the day of sham-irradiation. Animals were subsequently tested for 2 hours per day for 3 days. Subjects were monitored by closed-circuit television for changes in gross performance and for postirradiation emesis. Performance for the first 2 hours postirradiation was also video-taped for later analysis.

2.3.4 Data Collection.

The rate of rotation and the number of revolutions were permanently recorded on strip charts. Postirradiation performance was subsequently analyzed for each 10-minute work session to determine the number and duration of incapacitations and the performance levels when working. Subjects were considered incapacitated if no rotations of the wheel occurred for at least 1 minute. The subjects were considered recovered when they continuously rotated the PAW at any speed for 1 minute. The video recordings were later reviewed to determine time to emesis, duration of emesis episodes, and time to PCI or death.

2.4 IRRADIATION CONDITIONS.

Subjects were exposed to mixed neutron-gamma radiation from a research reactor (Training Research Isotopes General Atomic:

TRIGA) at the Armed Forces Radiobiology Research Institute (Sholtis, 1981). The reactor was operated in the pulsed mode, delivering the radiation dose with a 10-millisecond (full width at half maximum) time interval. The VDT subjects exposed in the unmoderated TRIGA reactor field were positioned so that the vertical midline of the subject was 100 to 200 cm from the centerline of the reactor core depending on dose required, with the animal facing away from the reactor. The unmoderated field has a free-in-air (FIA) neutron-to-gamma kerma ratio of 4:10, and neutron and gamma spectrum average energies of 0.8 and 1.5 MeV, respectively. A 5-cm thick lead shield when positioned between the reactor and a subject results in a free-in-air neutron-to-gamma kerma ratio of 3:1, with neutron and gamma spectrum average energies of 1.0 and 1.4 MeV, respectively. All VDT and PAW subjects studied with neutron-to-gamma fields of 3:1 were positioned so that the vertical midline of the subject was 90 cm from the centerline of the reactor core, with the animal facing away from the reactor. In both the 3:1 and 4:10 fields, the chaired VDT subjects were placed in an isolation chamber constructed of 2-cm thick plywood with the reactor side (back) cut away. The PAW subjects were restrained in an attached Plexiglas box prior to their entry into the physical activity wheel (Figure 2-2).

2.5 DOSIMETRY.

To relate free-in-air (FIA) kerma in the reactor to exposure values in the battlefield, three steps are required: (a) accurate values of tissue dose and neutron-to-gamma ratio at the midhead of a monkey in the reactor, (b) estimates of FIA dose and spectra at a series of distances from typical nuclear weapons, and (c) folding of the battlefield spectra with a model of man to obtain estimates of tissue doses and neutron-to-gamma ratios at the midhead.

2.5.1 Reactor Field and Doses.

Dose measurements were made by two AFRRI physicists, K. Ferlic and E. Daxon (Zeman, 1984) using paired 0.5-cm^3 ionization chambers at midline within a monkey phantom positioned in either a chair or in the restraining box on the wheel. The paired ionization chambers were those described in (ICRU, 1978). One chamber had A-150 plastic walls and was filled with tissue-equivalent (TE) gas; the other had magnesium walls and was filled with argon. The phantom trunk was a Plexiglas cylinder (10-cm diameter by 33-cm tall) filled with TE liquid. The head section consisted of four 3-cm thick disks of TE plastic with diameters of 9, 10, 10 and 8 cm, respectively, from top to bottom. For the PAW models, legs were added in a position that modeled a monkey sitting in the restraint box. Each leg for the phantom consisted of two Plexiglas cylinders; one 5cm in diameter and one 3cm in diameter, and both 18cm long.

These measurements gave the midhead and midthorax neutron and gamma doses associated with the external FIA measurements in the reactor. The neutron-to-gamma ratio of the unmoderated free-in-air field at 1 meter from the reactor core was shown to be 4:10. When 5 cm of lead was interposed between the subject and the reactor core, the neutron-to-gamma ratio was 3:1, and when 15 cm of lead was used as moderator, the neutron-to-gamma ratio was 10:1. The neutron-to-gamma ratio increases as the thickness of the moderator increases because lead is very effective at stopping gamma radiation, but has less effect on the neutrons. These moderators also affect the shape of the spectra that reach the phantom, because the more energetic gamma rays penetrate the lead in greater abundance. Thus with the 5 cm of lead, the midhead would receive 7.5 times the dose from neutrons relative to the total dose as it would in the unmoderated field.

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The two radiation environments for this study were neutron-to-gamma ratios of 3:1 and 4:10 FIA, which become neutron-to-gamma ratios of 1.6:1 and 3:10, respectively, at the midhead of the average monkey. The neutron-plus-gamma dose at the midline thorax position was taken as the defined dose for all experiments.

Propagation of error analysis indicated uncertainties of 8 percent on total dose and 18 percent on neutron-to-gamma ratio in addition to the uncertainties associated with individual animal size and weight variation. A summary of the doses and animals tested is given in Table 3-1.

(Verbinski, 1981) undertook a major effort at mapping the dose field in the AFRRI reactor exposure rooms under a variety of conditions. A series of Monte Carlo Transport computations and one-dimensional (spherical) discrete-ordinate computations were made, starting with a mock-up of the reactor core and transporting through the appropriate moderator, animal-restraining device, etc. Careful dose measurements were made at a variety of locations for each configuration. Measurements of the neutron spectra were also made with activation foils for validation of the computed values. A 1984 study by (Kaul, 1984) used the Verbinski data and a phantom model to estimate doses at the surface and at midhead of a monkey in the reactors. This study validated the Daxon and Ferlic (Zeman, 1984) phantom dosimeter measurements.

A study done by Oak Ridge National Laboratory (ORNL) (Johnson, 1983) for AFRRI folded the spectra in the reactor with a model of a monkey head, and has provided neutron and gamma spectra inside the monkey's head as well as in the reactor. The measurements made by Ferlic and Daxon (Zeman, 1984) provide good experimental estimates of the neutron-to-gamma ratio at the midhead of the monkey in the reactor; the ORNL study has provided reasonable spectra for the same locations.

2.5.2 Battlefield Relevance of Irradiation Doses.

The ORNL Engineering Physics Division also computed free-in-air (FIA) neutron-to-gamma fields and doses at a series of distances from a battlefield nuclear detonation. They used the ATR4 code and folded the resulting spectra with a previously developed midhead radiation dose-response function (Trubey, 1979). This provided AFRRI with a set of paired values of FIA dose and midhead dose to man for both neutron and gamma radiation expected in nuclear combat. A similar set of paired values was provided by Science Applications International, Inc. (SAI) from dosimeter-verified computations of an early nuclear device (SAI, unpublished) detonated on a steel tower and SAI's model of man. The proportions of gamma radiation and neutrons per dose in these two separate studies were very different because the two detonations were of different yields. But when the logarithm of total dose (neutron plus gamma) FIA is plotted against the logarithm of midhead total dose for man, a remarkably linear relationship exists. Furthermore, the same relationship exists for both sets of data, and the resulting function is:

$$\log \text{dose FIA} = \frac{\log \text{dose midhead} + 0.14743}{0.98506} \qquad (2.1)$$

The coefficients were obtained by the least squares method using data from both ORNL and SAI.

Actual animal irradiations were monitored with ionization chambers, and sulphur foils were mounted at fixed positions near the reactor core and on the chair or Plexiglas restraining box, in order to provide corrections for reactor output variations. The measured values obtained by these dosimeters were converted to dose to the midhead of monkeys using the (Zeman, 1984) study. Finally, equation 2.1 permitted FIA kerma in the battlefield to be calculated for each of the monkeys in this study.

Examination of the FIA neutron-to-gamma ratios and spectra from several unclassified sources (Loewe, 1983; Kaul, 1984; Kaul, 1983; DNA, 1975; Marcum, 1982), at distances that yielded 2000 cGy total FIA doses for the same devices showed large differences in the neutron-to-gamma ratios for evaluations done by different groups. These differences were attributable to different computational methods; e.g., Monte Carlo versus ATR approximations, different assumed environmental and soil conditions, different assumed burst height, and an older nuclear device tested on a tower versus a contemporary weapon presumed over ground. This brought into question the neutron-gamma ratios and spectra and doses applicable to these studies.

In order to resolve the disparities, a contract was awarded by DNA to evaluate neutron and gamma spectra for five currently deployed weapons under the same conditions at burst heights appropriate for the weapons yield (SAI, unpublished). SAI used state-of-the-art computation techniques including "fireball gamma" components, and evaluated the doses, neutron-to-gamma ratios, and spectra at a variety of dose points. They folded the spectra with their model of man and computed the neutron and gamma spectra and doses midhead and midthorax at the same FIA dose points.

Using the data resulting from this contract (SAI, unpublished), it is possible to select a particular nuclear weapon with its own dose-versus-distance and neutron-gamma-distance characteristics, and in conjunction with the incapacitation data in this report to select the particular curve of incapacitation versus time for any dose and the neutron-to-gamma ratio that is associated with it.

SECTION 3
ANALYSIS OF PRIMATE INCAPACITATION DATA

3.1 PREVIOUS ANALYSIS.

Incapacitation in monkeys and other animals following supralethal doses of ionizing radiation has been studied at the Armed Forces Radiobiology Research Institute (AFRRI) since 1965. In the earliest study at AFRRI specifically of incapacitation, 10 animals were irradiated at 13 midline tissue dose levels from 2500 to 80000 cGy, and the time to PCI and death was recorded (Seigneur and Brennan, 1966). Subsequent studies at AFRRI observed the ETI of trained monkeys after a single dose of radiation (Curran et al, 1971, 1973, 1974; deHaan et al, 1968, 1969; Franz et al, 1968; Germas et al, 1969; and Young and McFarland, 1970) after multiple doses (Germas and Shelton, 1969; McFarland and Young, 1971) and after partial-body irradiation (McFarland, 1971; Thorp, 1969).

The first attempt at an overall analysis of the AFRRI data on incapacitation as a function of time was made by (Warshawski, 1975, 1976) of the U S Army Nuclear and Chemical Agency (USANCA). At the time of his analysis, 36 monkeys had been tested and evaluated at the N/g = 4:10 ratio, and 9 had been tested at the N/g ratio of 3:1. Warshawski calculated a dose at which 50 percent of the animals were effected (ED_{50}) versus time, for use in the development of Army field manuals.

In 1973 data from previous AFRRI studies (at N/g = 4:10) on a total of 88 monkeys that had been trained on a visual discrimination task were assembled and analyzed (Curran et al, 1973). These animals were tested at doses from 1100 to 15000 cGy midline tissue dose, equivalent to 1500 to 17335 FIA cGy. Their analysis was in terms of latency and percent correct. Graphs of

latency and percent correct versus time show a distinct degradation at 7 to 20 minutes postirradiation. A dose-response relationship was not attempted in this study. Later, R. Young and S. Levin of AFRRI computed dose-response (probit) curves for monkeys tested at N/g = 3:1 and 4:10 for a comprehensive 2 hour analysis. In this analysis, if an animal was unable to perform for at least 1 minute during the first 2 hours postirradiation, the animal was considered to be incapacitated. Plots of percent response versus dose on log-probit paper were reasonably linear, and showed that gamma radiation was more effective at producing incapacitation than was neutron radiation. The results of these analyses were presented to NATO and U.S. military symposia but were not published.

When digital computers with large capacity disc storage became available at the AFRRI, (Franz 1981) stored all of the minute-by-minute data on the performance of irradiated monkeys, listed in Table 3-1, was stored in a single database. At the same time, a data management system and a number of automated systems for the analysis of parts of these data were developed. (Franz, 1985) used the data base in the calculation of comprehensive two-hour dose response functions (probits) for monkeys performing the physical activity wheel task.

The irradiated monkey database and software made it possible to carry out the minute-by-minute analyses on the 141 VDT monkeys tested at N/g = 4:10, the 52 VDT monkeys at N/g = 3:1, and the 39 PAW monkeys at N/q = 3:1 presented in this report.

Table 3-1. Median doses and numbers of monkeys tested.

N/g=4:10 (VDT)		N/g=3:1 (VDT)		N/g=3:1 (PAW)	
Med. Dose FIA cGy	Number tested	Med. Dose FIA cGy	Number tested	Med. Dose FIA cGy	Number tested
1233	28	2104	11	1627	3
1806	19	2464	10	2216	9
2938	41	3380	11	2562	8
5987	27	4441	10	2913	7
7247	14	5612	10	3653	2
12755	5			5874	10
17355	7				
Total Tested	141		52		39

Median values are given because the actual dose delivered by the pulse reactor is within ± 5% of the requested dose.

3.2 MINUTE-BY-MINUTE ANALYSIS OF VISUAL DISCRIMINATION TASK DATA.

The concept of incapacitation as applied to military planning includes early transient and permanent complete incapacitation, because the military needs to know the percentage of individuals able to perform at a given time after exposure to ionizing radiation. An animal's response is interpreted as incapacitated if it does not respond to six consecutive 10-second trials. If the animal subsequently responds correctly for 1 minute, it is considered to have recovered. A minute-by-minute 2-hour time history was created for each animal showing whether the animal was able or unable [up (0) or down (1)] to perform the assigned task. After the initial 2 hour period, the VDT animals were tested and data recorded for 17 minutes each hour until 8 hours postirradiation. From 9 hours until 24 hours, the animals were tested for 17 minutes, every other hour. After 24 hours the animals were observed until PCI.

In the N/g = 4:10 group, 141 VDT animals were exposed and tested at seven dose levels, with doses ranging from 1050 to 17570 cGy 3:1 radiation field at doses ranging from 1825 to 5820 cGy FIA.

The 60 day median lethal dose ($LD_{50/60}$) for monkeys at N/g = 4:10 in the reactor is 579 cGy FIA; thus the doses are 2 to 30 times the LD_{50}.

3.2.1 Fitting Probit Lines to Dose Versus Incapacitation.

The minute-by-minute histories were aggregated in one minute groups. Each minute in the N/g = 4:10 data contained a set of 141 0 or 1 discrete values; each discrete value was associated with the dose to which the animal had been exposed. W. Jackson of AFRRI developed a computer program based on a method proposed by (Finney, 1978), in order to fit a probit line to the dose-response data at each minute.

The probit computation assumes that there is a Gaussian distribution of sensitivicies of individuals to radiation, i.e.; an individual is sensitive to an exact dose that is just sufficient to produce incapacitation. Each individual has a different sensitivity, and the ensemble of the sensitivities of all individuals to a given dose would have a Gaussian distribution. Often, the distribution of sensitivities is not Gaussian; instead, the logs of the doses or some other transformation applied to the doses has a Gaussian distribution. An additional assumption is that if a certain dose (say, 3000 cGy) would cause an incapacitation in an individual, then any larger dose would also cause an incapacitation to that individual.

There is no direct way to determine an individual's sensitivity because the radiation cannot be titrated. Instead, a group of animals is exposed (one at a time) to a particular dose, and the percent that are incapacitated is determined. Then another group is exposed to another predetermined dose, and the percent that are incapacitated is determined, and so on. From the several dose

groups and the associated responses, a dose-incapacitated plot can be made (see Figure 3-1) on probit graph paper. This graph paper has an ordinate scale in units of percent, spaced according to a Gaussian transformed scale. This scale is such that a cumulative Gaussian histogram will plot as a straight line. The abscissa is in units of dose or transformed dose. Because the animals were exposed in a pulsed reactor, the exact dose called for was seldom achieved; therefore, each non-overlapping interval in the plot contains a range of doses, and the percent incapacitated are plotted against the median dose of the intervals.

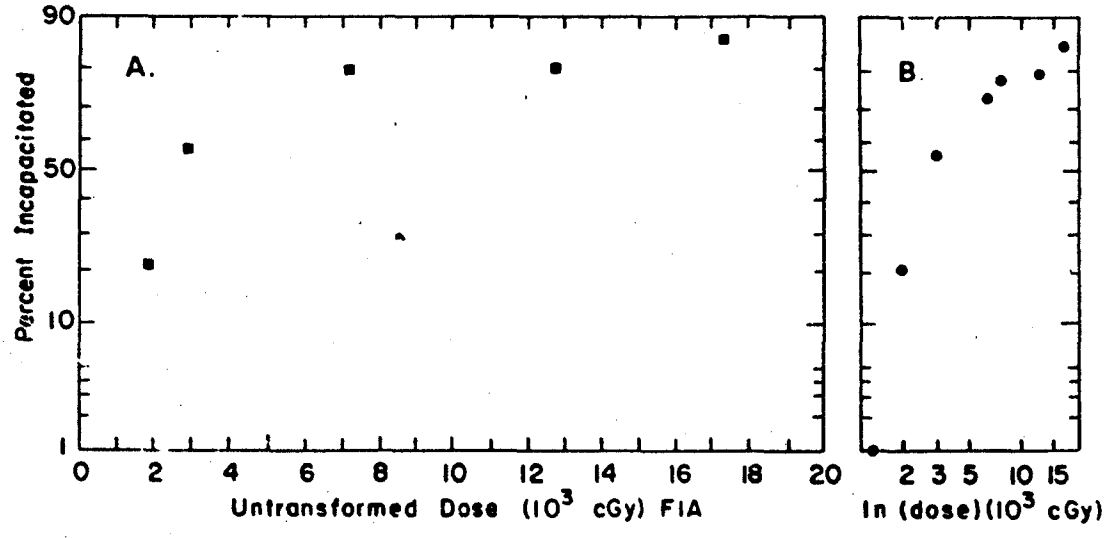


Figure 3-1. Percent incapacitated at 5 min versus (A) untransformed and (B) ln dose for the N/g = 4:10 field on probit graph paper.

3.2.2 The Box-Cox Transformation.

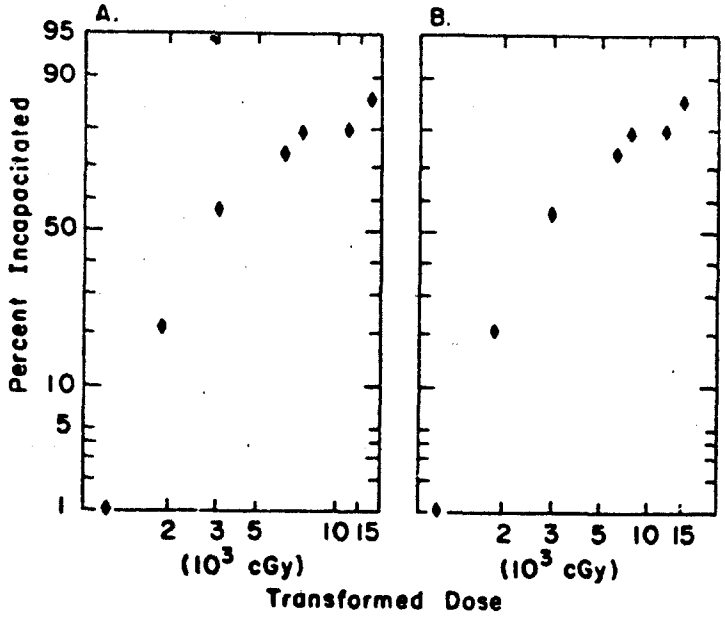
Examination of the data at 5 minutes (Figure 3-1) shows that the untransformed points do not follow a straight line (a), and that the use of a logarithmic transformation does not linearize the plot (b); however, a generalized transformation, which was proposed by (Box and Cox, 1964), does linearize the data.

This transformation has the form:

$$D^* = \frac{(D - K)^L - 1}{L}$$

where D* is the transformed dose, D is the original unit dose, K is a parameter that limits the lowest value that D can take, and L is a general shape parameter.

In this transformation, when K = 0 and L = 1, the D* is in the original units and when L = 0, D* becomes the natural log transformation. This transformation was applied to the N/g = 4:10 data for 5 minutes postirradiation, and figures 3-2 and 3-3 show that as the parameter L becomes more negative (L = -0.1, -0.2, -0.4), for K = 300, data points become increasingly linear.



(A) L = -0.1, K = 300 (B) L = -0.2, K = 300

Figure 3-2. Box-Cox transformation of the dose for VD1 N/g = 4:10 field

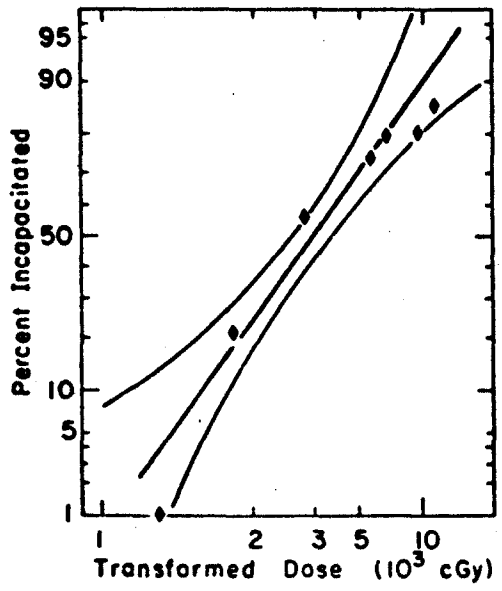


Figure 3-3. Box-Cox transformation of the dose for VDT N/g = 4:10 field using L = -0.4, K = 300, and with 95 percent confidence bands.

Figure 3-4 shows the untransformed data at 5 minutes post-irradiation for N/g = 3:1. Figure 3-5 shows that the same parameter values (K = 300 and L = -0.4) in the Box-Cox transformation effectively linearize these data as well as the N/g = 4:10.

Similar plots made for 10, 20, 30 and 60 minutes show that these same values of the parameters of the transformation appear to linearize the data for the other times as well. Using this transformation and then computing a probit line using all 141 observations for each minute of data available, it is possible to evaluate the probit functions numerically and obtain a predicted value of percent incapacitated for any dose at each time point.

The use of probits allows the computation (prediction) of values at any selected dose, so that curves for N/g=3 can be compared with curves for N/g=4 although the doses at which animals were tested are different. The probit method provides confidence intervals for points on the line, and insures that the responses will be monotonic functions of dose, i.e., a higher dose must not result in a lower number incapacitated, and hence the curves for different doses do not overlap.

Figures 3-3 and 3-5 show 95 percent confidence bounds for percent incapacitated about the entire predicted probit lines for the N/g = 4:10 and N/g = 3:1 data, respectively, at 5 minutes. The width of the confidence interval, which is minimal at the 50 percent point, depends on the sample size as well as the variability of the data; therefore, it is not surprising that the interval for the N/g = 4:10 data, containing 141 animals, is much narrower than the interval for the N/g = 3:1 data, which has a total of 52 points.

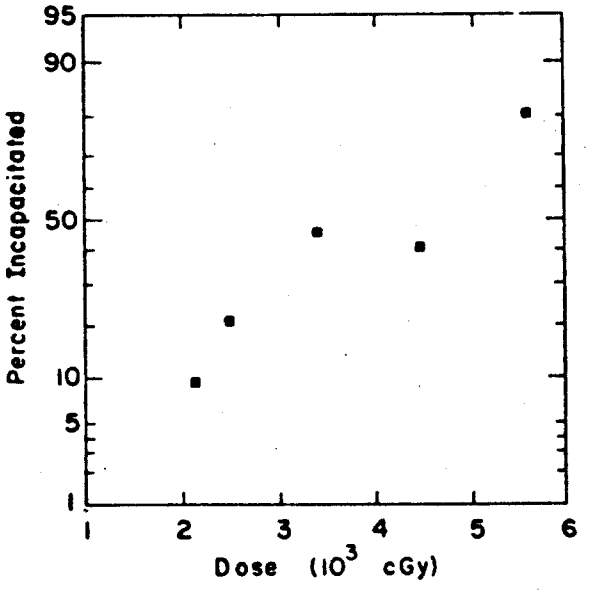


Figure 3-4. Percent incapacitated at 5 min versus untransformed dose for the N/g = 3:1 field.

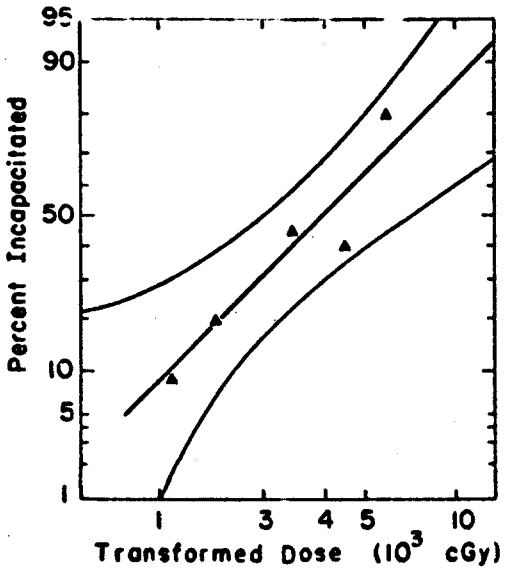


Figure 3-5. Percent incapacitated at 5 min versus Box-Cox transformation of the dose for the N/g = 3:1 field using L = -0.4, K = 300, with 95% confidence bands.

Figures 3-3 and 3-5 and the data from which they are derived also permit us to compare the observed percentage incapacitated with the value predicted by the probit line. Comparison of the observed with the predicted values at 5, 10, 20 and 60 minutes, using the chi-square test of significance, shows that the probit line was a "good fit" to the data. These tests were repeated for the visual discrimination task data at N/g = 4:10 and N/g = 3:1, and for the PAW data for N/g = 3:1; none were rejected as not fitting well.

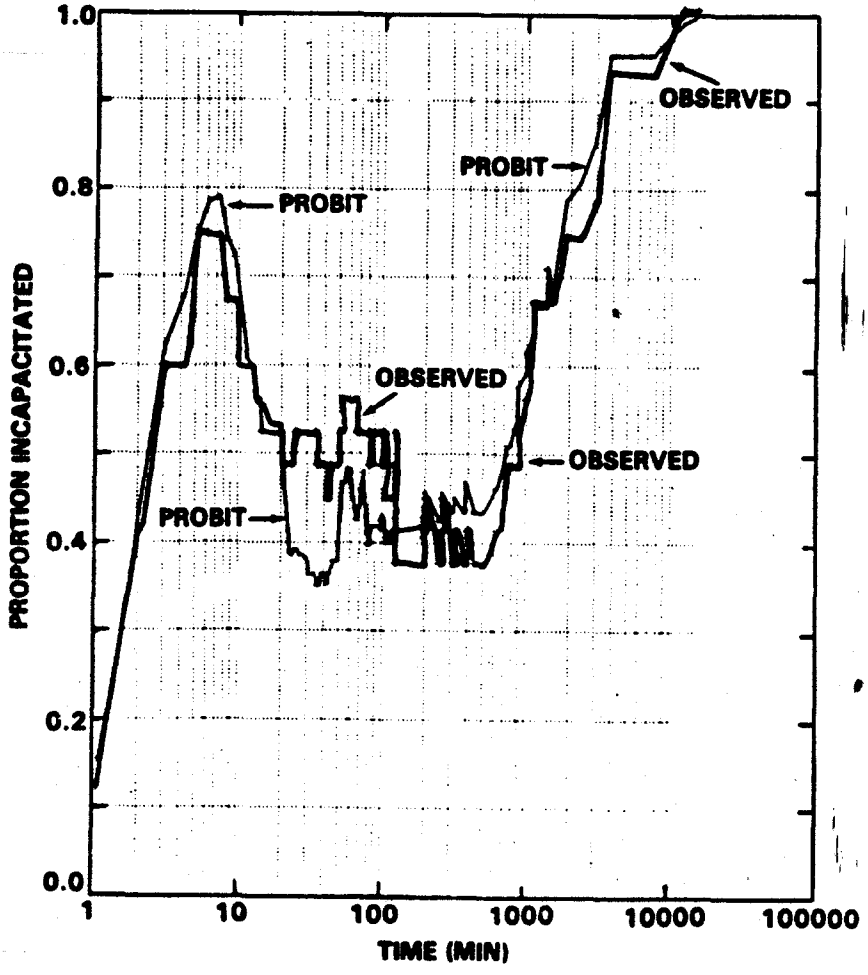


Figure 3-6. Observed and probit predicted proportion incapacitated versus time (minutes postirradiation) for the VDT at 5990 cGy (FIA) N/g = 4:10 field.

To compare observed and predicted values over time, two doses were selected for the N/g = 4:10 set of data: 5990 and 1800 cGy FIA. The observed proportion of the 27 animals incapacitated at a median dose of 5990 cGy and the observed proportion of the 41 at 1800 cGy were plotted for each time point and connected.

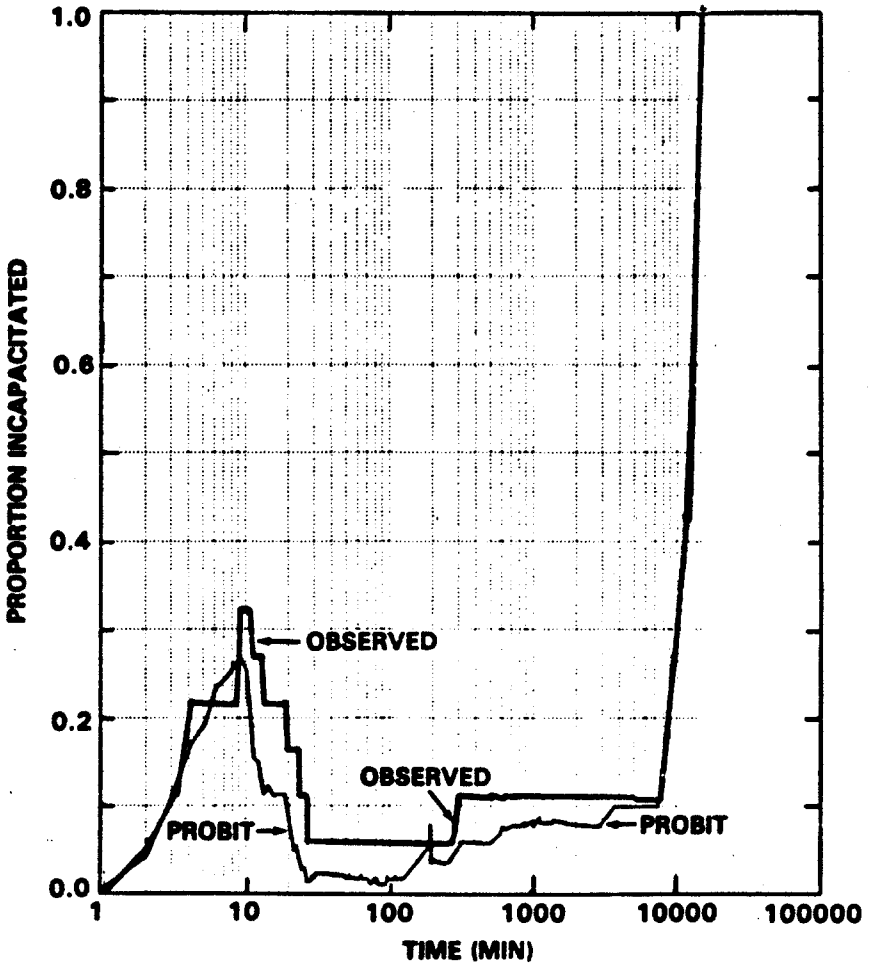


Figure 3-7. Observed and probit predicted proportion incapacitated versus time (minutes postirradiation) for the VDT at 1800 cGy (FIA) N/g = 4:10 field.

The minute-by-minute probit lines were also evaluated at 5990 and 1800 cGy, and the proportions incapacitated for each minute are also plotted in Figures 3-6 and 3-7 as a series of connected dots. Comparison of the probit and observed curves shows relatively small differences over the range of times.

3.2.3 Families of Curves.

Values of proportions incapacitated versus postirradiation time have been computed at a range of doses within which incapacitation is known to occur. The doses selected for evaluation and plotting are 1000, 1500, 2000, 2500, 3000, 5000, 8000 and 15000 cGy FIA for both N/g groups. The highest dose at which the N/g = 4:10 group (Figure 3-8) animals were tested was 17570 cGy FIA. Although the N/g = 3:1 subjects (Figure 3-9) were tested only at doses up to 5825 cGy FIA, the probits have also been evaluated at 8000 and 15000 cGy, and are shown only for comparison with the 4:10 group. The 15000 cGy extrapolation is shown dotted. The 1000, 1500 and 2000 cGy curves are shown as heavy dashed lines because extension beyond 1000 minutes is based on cumulative proportion PCI as there were not enough survivors to compute probits at those times.

The graphs of these data in Figures 3-8 and 3-9 show curves of proportion incapacitated versus time for eight doses from 1000 to 15000 cGy. If standard errors were presented for each point, a confused figure would result, hence standard errors are only presented for the predicted 2000 cGy and 15000 cGy doses at 5, 30, 60 and 300 minutes, which fall near or on peaks and valleys. Examination of the standard errors gives some idea of whether the peaks and valleys are "real". The conventional statistical tests which compare peaks and valleys are not applicable, because observations on the same animals are used for the probits at each minute causing the groups to be highly correlated.

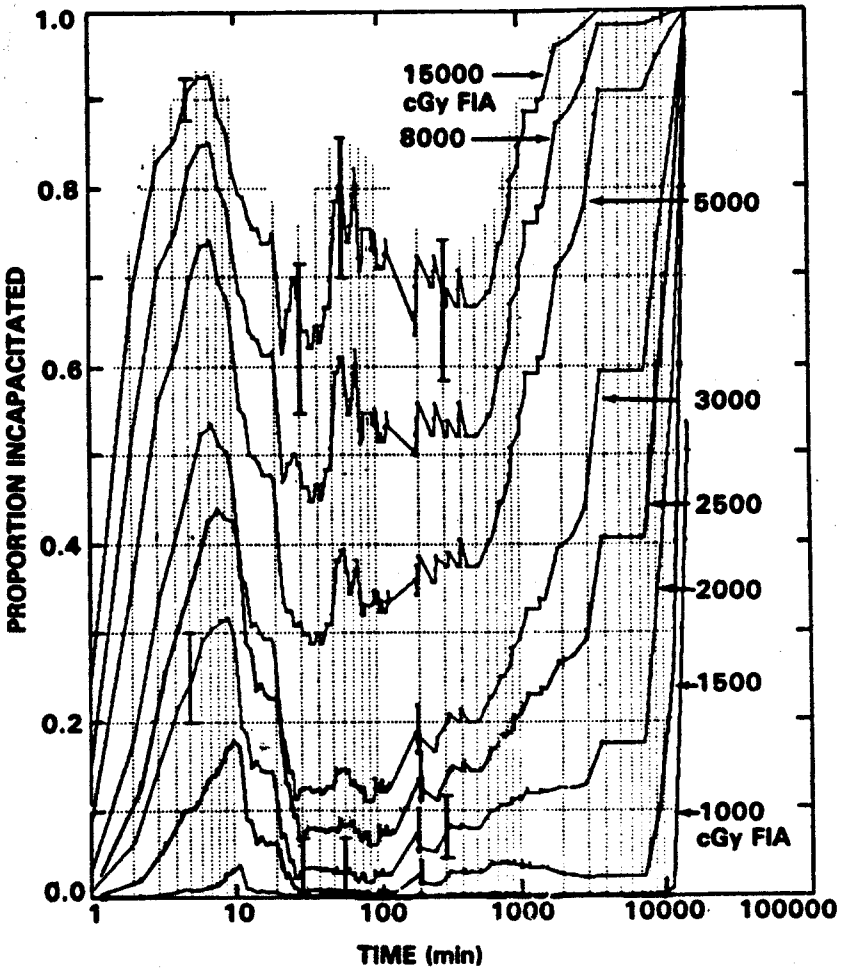


Figure 3-8. Proportion incapacitated versus time (minutes postirradiation) for the VDT N/g=4:10 field.

These curves describe the phenomenon of incapacitated in terms of the proportion of individuals, at a given dose, that would be incapacitated as a function of time. The data used to obtain these results represent the entire pool of applicable data on nonhuman primates. Very little liberty has been taken with those data as the use of best fitting probits for interpolation between doses represents a minimal manipulation of the data.

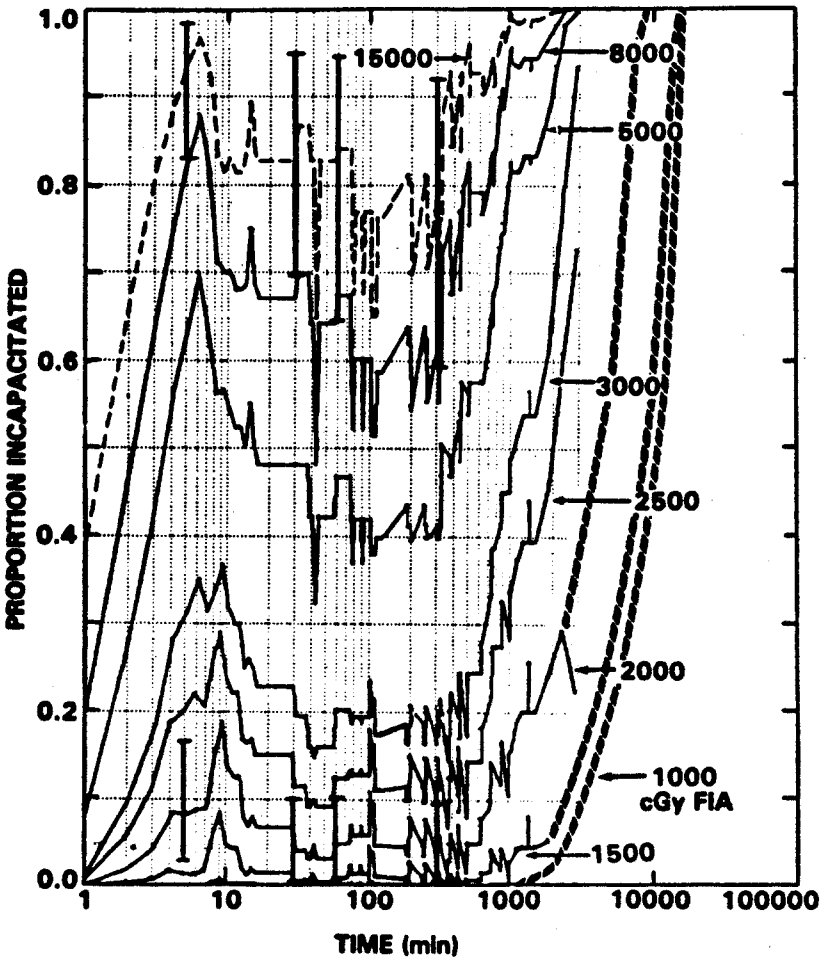


Figure 3-9. Proportion incapacitated versus postirradiation time for the VDT N/g=3:1 field.

Evaluation of the probits at a series of times permits the trend of the proportion incapacitated to be observed. The results also represent the probability of occurrence of an event, and the confidence intervals attempt to bound these. Estimates of the proportion incapacitated (or the probability of incapacitation) are required for military planning, and best available estimates of the probability are required regardless of the variability.

3.2.4 Smoothing Across Time.

Up to this point, these data have been "smoothed" only across dose by fitting a probit function to percent incapacitated versus dose for each minute; they have not been smoothed across time which would make the trend much clearer.

The method of decomposition developed by W. Jackson of AFRRI (described in the appendix of this report) results in a heavily smoothed curve that accurately "tracks" the trends, yet completely removes the small, minute-by-minute fluctuations. These small fluctuations are clearly random because most of them are far smaller than the standard error of the data at the given time.

These smoothed curves for N/g = 4:10 and for 3:1 are presented as Figures 3-10 and 3-11.

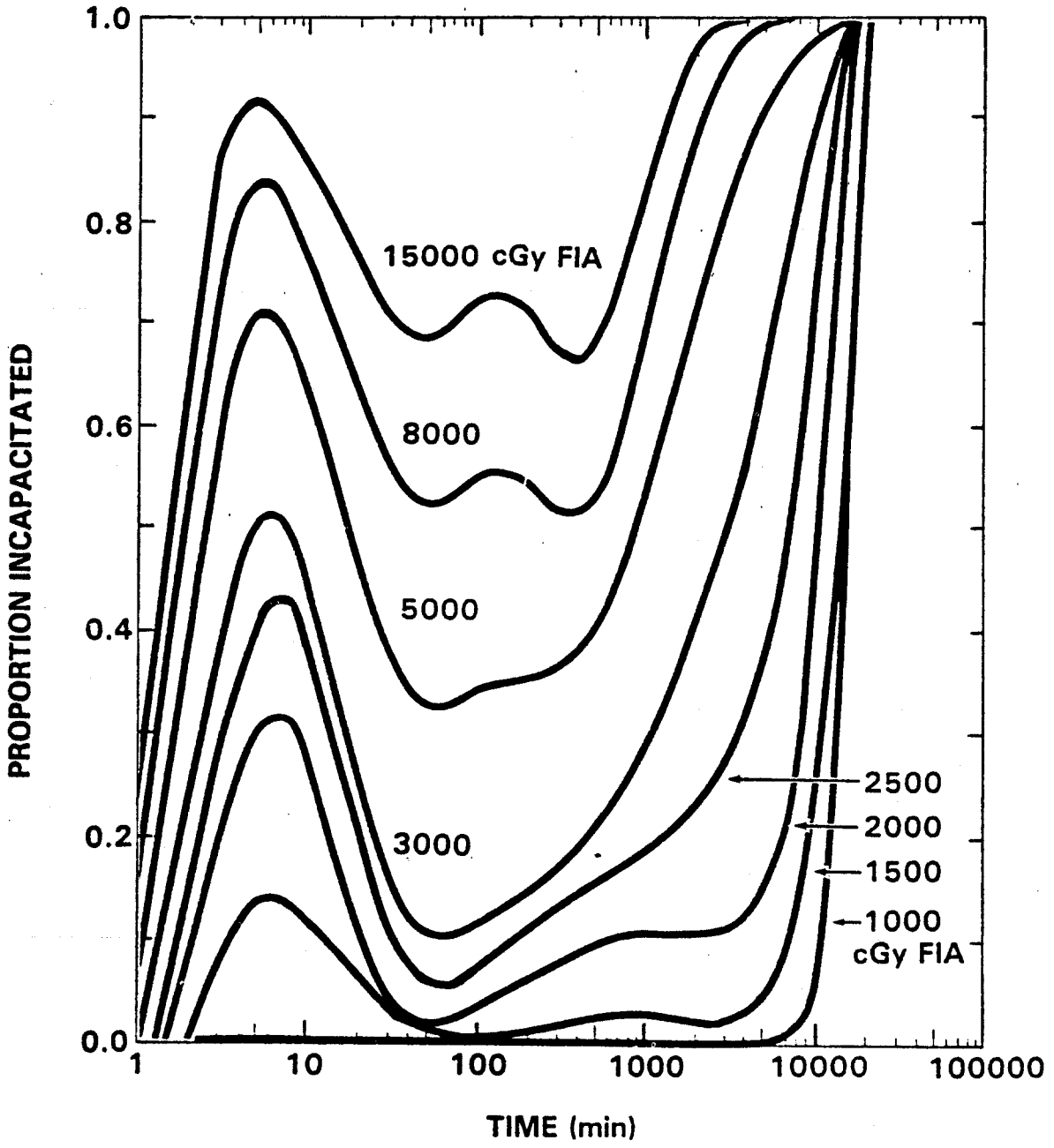


Figure 3-10. Smoothed proportion incapacitated versus time for the VDT N/g=4:10 field.

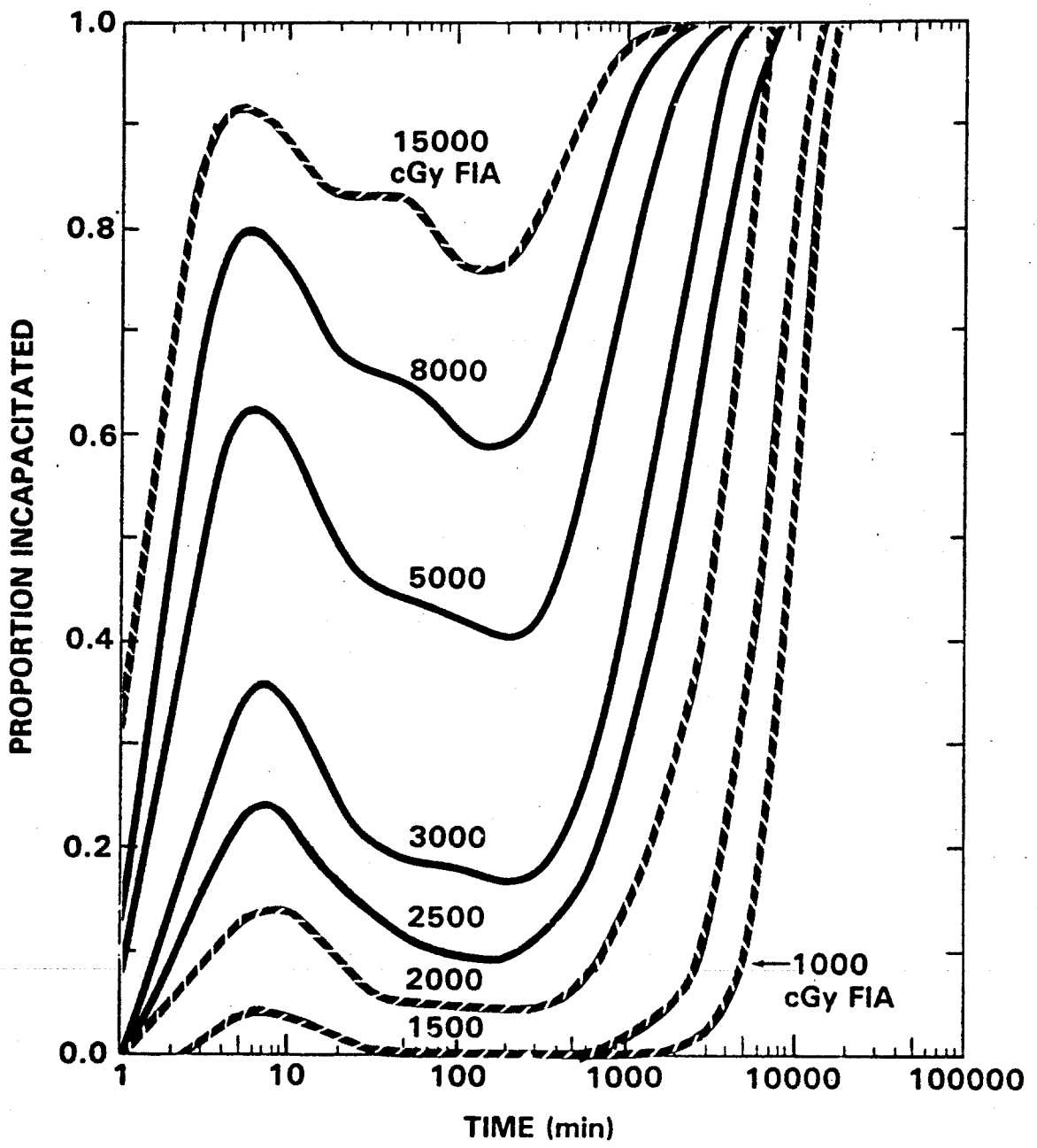


Figure 3-11. Smoothed proportion incapacitated versus time for the VDT N/g=3:1 field.

3.2.5 Variability of Original Data About the Smoothed Curves.

Two techniques have been applied to the data in order to smooth the final results: the probit smoothed across dose and the decomposition smoothed across time. Table 3-2 contains estimates of the total variability of the smoothed curves. The estimates of

Table 3-2. Percent Incapacitated From Final Smoothed Curves and the Values at +1 and at -1 Standard Error

2000 cGy FIA	VDT				PAW	
	N/q = 4:10		N/q = 3:1		N/q = 3:1	
Time Post-Irradiation Min	Incap %	%+1SE %-1SE	Incap %	%+1SE %-1SE	Incap %	%+1SE %-1SE
5	31.1	39.7 23.4	12.5	23.8 5.6	14.0	31.0 4.8
10	27.5	35.2 20.7	13.7	24.7 6.7	19.0	37.5 7.5
20	11.8	18.0 7.3	9.2	19.1 3.7	11.9	28.1 3.7
30	5.3	10.2 2.5	6.3	15.1 2.1	6.3	17.3 1.7
60	2.4	5.3 1.0	4.7	11.6 1.5	3.4	13.9 .5
120	4.2	8.7 1.8	4.8	12.1 1.5	4.3	13.5 .9

5000 cGy FIA	VDT				PAW	
	N/q = 4:10		N/q = 3:1		N/q = 3:1	
Time Post-Irradiation Min	Incap %	%+1SE %-1SE	Incap %	%+1SE %-1SE	Incap %	%+1SE %-1SE
5	71.3	77.1 64.9	62.3	72.3 51.4	57.7	71.9 42.3
10	62.3	68.6 55.6	58.4	68.6 47.6	68.9	81.4 53.8
20	45.2	52.0 38.6	48.6	59.4 37.9	56.1	70.8 40.5
30	37.1	44.0 30.7	45.6	59.5 37.8	41.5	56.9 27.4
60	32.4	39.0 26.3	43.3	54.2 32.9	19.7	34.2 09.7
120	34.7	41.5 28.4	40.9	51.9 30.6	42.6	58.1 28.1

variability were obtained at 5, 10, 20, 30, 60 and 120 minutes by adding the variance of the probit line (in probit units) to the variance of the probit points about the smoothed curve at the same time points. The variances may not be converted back to original units because of the nonlinearity of the transformation, but the ±1 standard error about the mean points have been calculated and converted back to the original percentage units.

These tables reflect the general relationship of the variability about the probit line, because that is the dominant component of variance. The width of the +1 SE to -1 SE interval is generally smallest around the 50 percent incapacitation value, and gets larger around the small and large percent values. The standard error reflects the variability of the observed values about the fitted probit line and the number of observations as well as the variability of the calculated probit point about the final smoothed value.

In general, this leads us to say that for a particular percent incapacitated, the standard errors of the 4:10 VDT (141 animals) is the smallest value, with the 3:1 VDT being larger, and finally the 3:1 PAW data showing the widest spread.

3.3 ANALYSIS OF PHYSICAL ACTIVITY WHEEL TASK DATA.

3.3.1 Definition of Incapacitation.

The physical activity wheel (PAW) permits the training, observation and remote continuous recording of data from a monkey performing a locomotor activity task (Curran et al, 1973).

An animal was considered incapacitated if it stopped turning the wheel for 60 consecutive seconds, i.e., one entire minute. They were considered recovered when they continuously rotated the PAW

for one minute at any speed. Previous studies (Curran et al, 1973, 1974) have described performance, including incapacitation, of PAW monkeys irradiated at 2500 and 5100 cGy FIA. A report by (Franz, 1985) describes the performance of a total of 39 animals irradiated at 1600 to 6100 cGy FIA at a N/g ratio of 3:1. In the Franz report these data were described in terms of an overall 2 hour incapacitation; i.e., if an animal was incapacitated for at least 1 minute during the 2 hours postirradiation, then it was said to have an incapacitation.

3.3.2 Similarity of Analytical Methods to VDT.

The analysis used for the PAW data is essentially the same as that used for the visual discrimination task (VDT): a minute-by-minute history of incapacitation (down) or function (up) is assembled for each animal. Then, using the ensemble of 39 animals, a dose-response function (probit) is calculated for each minute for the initial testing period of 6 consecutive hours. After the initial period, the monkeys were permitted to rest, and testing resumed for 2 hour periods at 24, 48 and 72 hours postirradiation. After that time, the animals were observed regularly, and the time to PCI or death was recorded.

The results of the minute-by-minute analyses of the PAW data are presented in Figures 3-12, 3-13 and 3-14. The proportion incapacitated in the PAW data varies from minute to minute far more than in the VDT data. This is because the animals that perform the VDT tend to have an incapacitation that is continuous and lasts 5 to 20 minutes, whereas the PAW animals tend to perform the task, stop, start again, and so on. These animals generally have 9 or more transient incapacitations, whereas the VDT animals tend to have 3 or less. The fact that there are only 39 animals in the PAW study, contributes to the variability, because the probit is less stable for a small sample size.

Because of the variability, the data for all four doses cannot be plotted on a single graph; they are shown in Figures 3-12 to 3-14. The final smoothed curves for 1000 to 8000 cGy are presented in Figure 3-15. The 1000 to 5000 cGy curves are solid but the 8000 cGy curve is dashed because it is an extrapolation. The 15000 cGy curve could not be reliably extrapolated because of the small sample size and large variability.

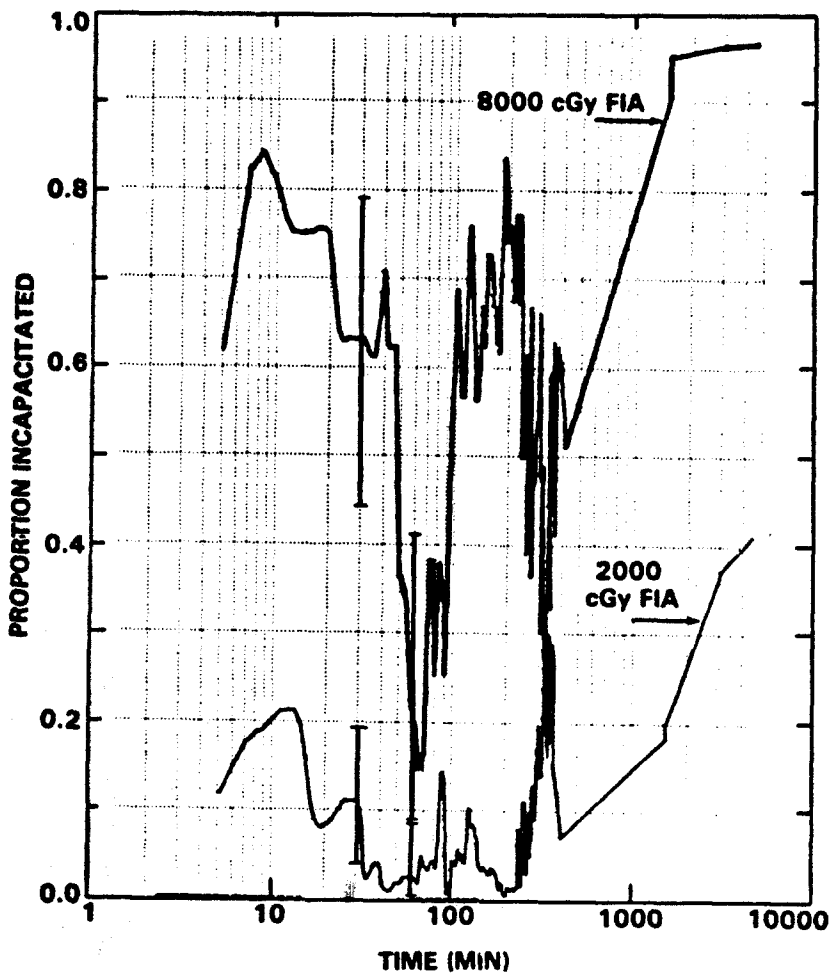


Figure 3-12. Proportion incapacitated versus time (minutes postirradiation) for the physical activity wheel at 2000 and 8000 cGy FIA in the N/g = 3:1 field.

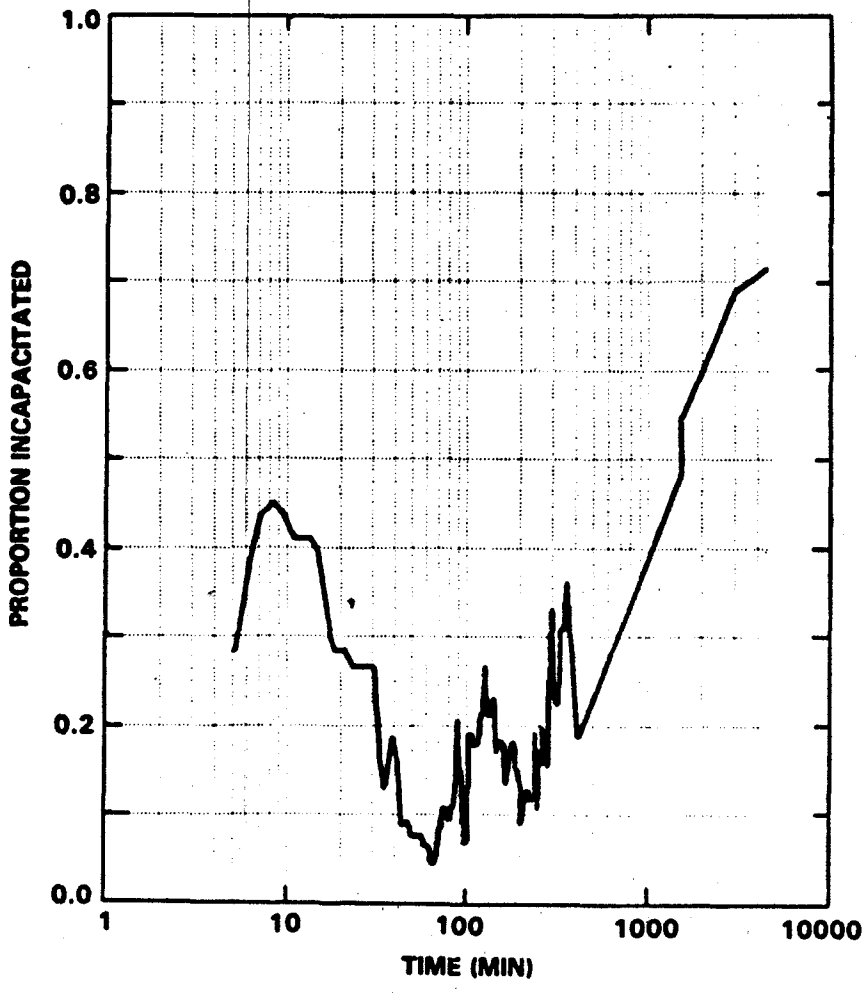


Figure 3-13. Proportion incapacitated versus time (minutes postirradiation) for the physical activity wheel at 3000 cGy FIA in the N/g = 3:1 field.

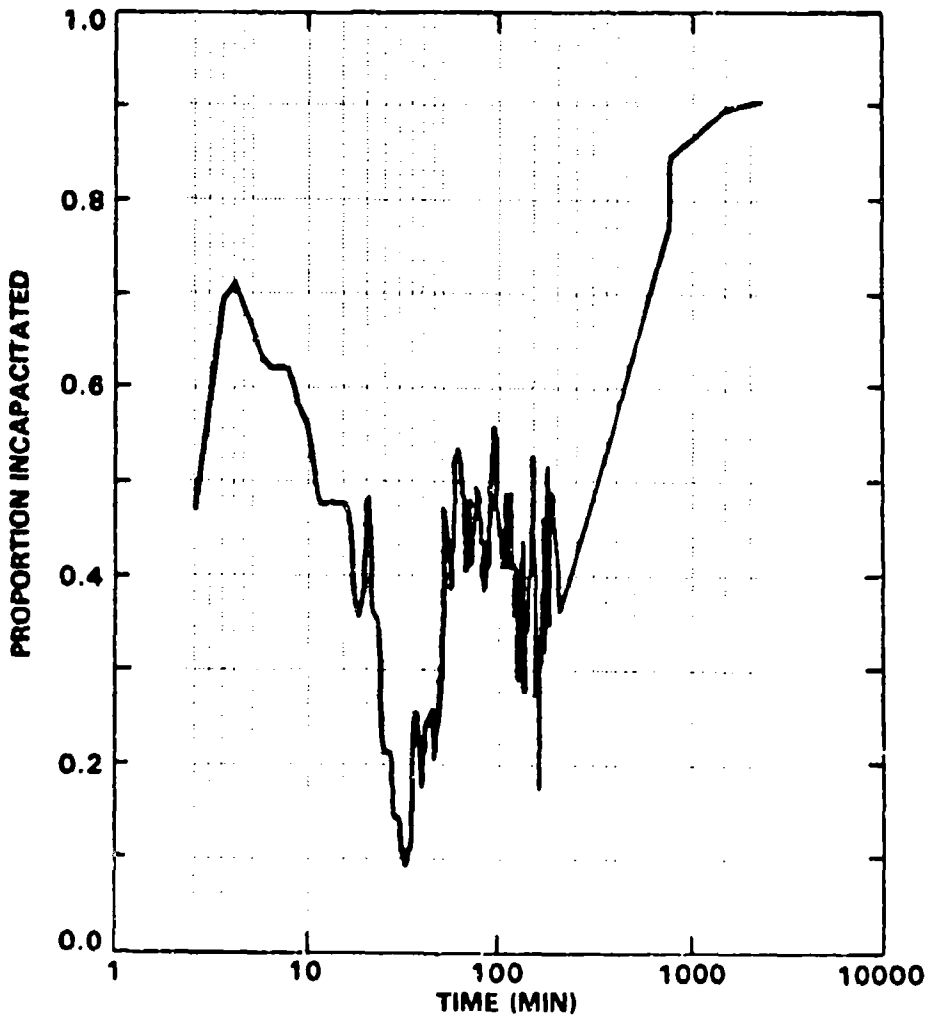


Figure 3-14. Proportion incapacitated versus time (minutes postirradiation) for the physical activity wheel at 5000 cGy FIA in the N/g = 3:1 field.

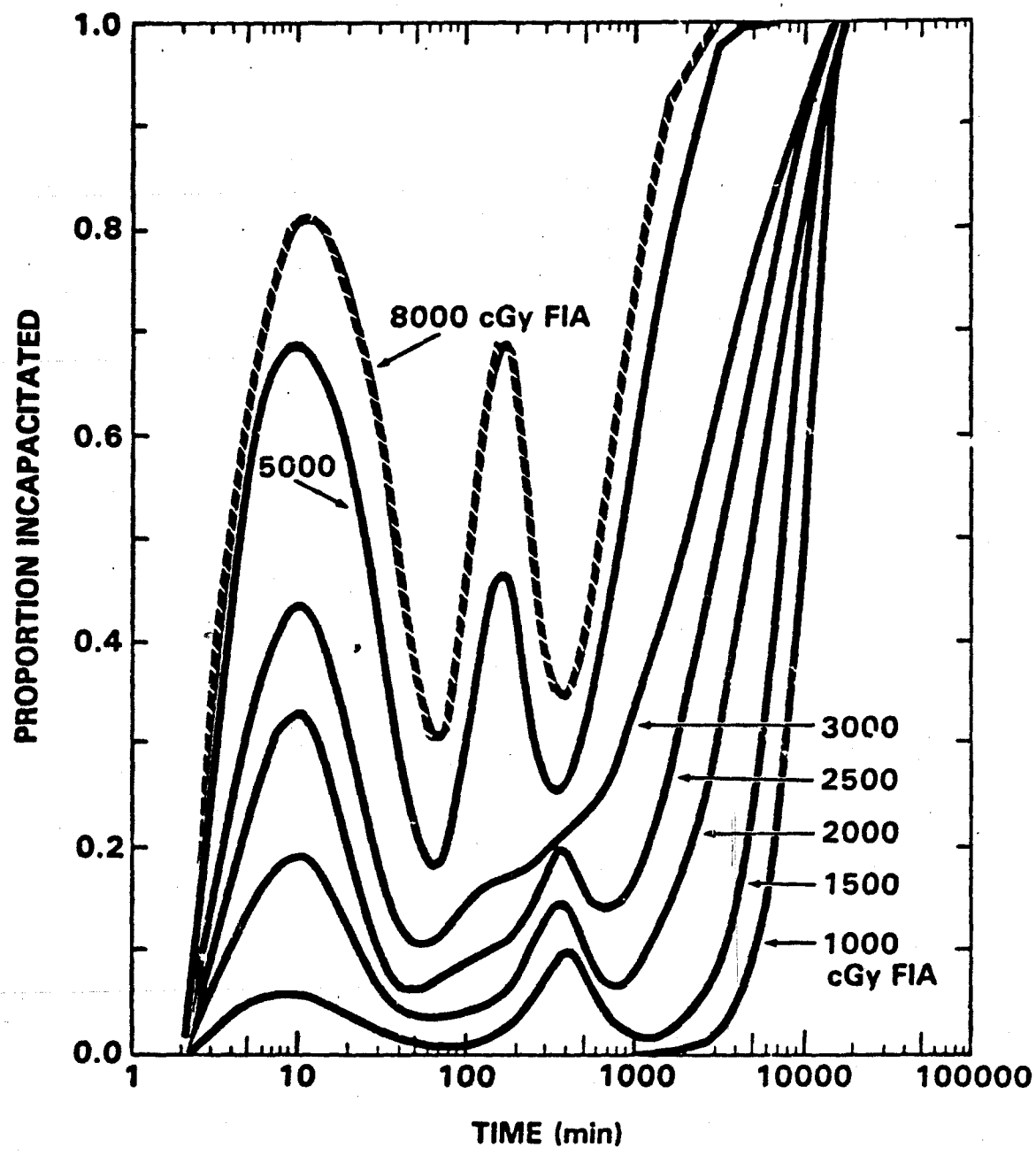


Figure 3-15. Smoothed proportion incapacitated versus time PAW in the N/g = 3:1 field.

SECTION 4
DISCUSSION

4.1 VISUAL DISCRIMINATION TASK.

The information in Figures 3-8 and 3-9 incorporates all known data on incapacitation of primates performing a visual discrimination task at neutron-to-gamma ratios of 4:10 and 3:1. Examination of these figures shows the proportion of individuals that were unable to perform their assigned task between the time of radiation pulse and 10000 minutes later. The curves in these figures show incapacitation for doses from 2000 to 15000 cGy FIA.

Transient recovery occurred earlier for the higher dose (5000-15000 cGy) animals, but a far lower proportion of those animals recovered than did those that received lower doses (2000-3000 cGy); 25 to 40 percent versus 85 to 95 percent, respectively. The higher dose animals tended to recover slightly earlier, if they recovered at all, and tended to PCI sooner than the animals that received a lower dose.

Comparison of the sets of smoothed curves for the data (Figures 3-10 and 3-11) shows that the patterns are similar. The proportion incapacitated at the higher doses are about the same (after <10min), but at the 2000 cGy and 3000 cGy doses, the animals irradiated at 4:10 show a higher percentage of early incapacitations. Recovery continued and reached a maximum (i.e., minimum incapacitation) at 100 to 500 minutes for the 3:1 animals.

The N/g = 4:10 animals had a peak transient recovery at 45 to 50 minutes postirradiation, with about 30 to 50 percent of the higher dose animals and 90 to 95 percent of the lower dose animals recovering. The higher dose animals in the N/g = 4:10

group tended to have a second incapacitation peak at about 150 minutes, at which time most of the lower dose animals were able to function satisfactorily.

By 2000 minutes (33 hours), 70 to 95 percent of the higher dose N/g = 4:10 animals were permanently incapacitated, while the same percentage of the high dose N/g = 3:1 animals were permanently incapacitated by 900 minutes (15 hours). Most of the N/g = 4:10 lower dose animals (2000-3000 cGy FIA) were permanently incapacitated by 5000 minutes (3.5 days), while the N/g = 3:1 animals were permanently incapacitated in less than 1 day at those doses.

4.2 PHYSICAL ACTIVITY WHEEL TASK.

Because the PAW tested animals were exposed at a N/g ratio of 3:1 (Figure 3-15), they can be compared to the VDT 3:1 data (Figure 3-11). The 15000 cGy dose curve is not included for the PAW data because extrapolation to that high dose results in unrealistic curves. Extrapolation to predict incapacitation at 8000 cGy is shown as a dashed line in Figure 3-15.

Comparison of Figures 3-11 and 3-15 for doses 2000 to 5000 cGy FIA shows that the early peak proportion incapacitated for the VDT and PAW animals were about the same, with the PAW animals reaching the peak a few minutes later than the VDT animals. Marked recovery (80 to 95 percent) is seen for the PAW animlas at about 1 hour. Some of the VDT animals recovered at about 1 to 2 hours, but a much smaller proportion (60 to 95 percent) of them recovered than did the PAW animals. The PAW animals had a secondary peak at about the time (2 hours) that the VDT animals were recovreing. Both groups show that the higher dose animals reached PCI earlier than the lower dose ones. The patterns of PCI are similar for the VDT and the PAW animals, with the VDT animals

reaching PCI at 20 hours and the PAW animals reached 80 percent PCI at about 30 hours. For 3000 cGy, the VDT animals reached 30 percent PCI at 40 hours as opposed to 92 hours for the PAW animals. At 2000 cGy, the VDT reached 80 percent PCI at 92 hours, while the PAW animals took 150 hours (6 days) to reach that PCI level.

4.3 MILITARY APPLICATION.

The radiation field inside a TRIGA reactor provides the closest approximation to a battlefield radiation field available as a laboratory research tool. The primates that were irradiated in this study performed tasks analogous to physically demanding and physically undemanding military tasks. While the tasks were not truly equivalent, they were at least representative.

The concept of behavioral incapacitation and, in particular, early transient incapacitation (ETI) provides a major source of objective data for targeting enemy forces with tactical nuclear weapons. Figures 3-10, 3-11 and 3-15 can be interpreted to show the proportion of enemy troops receiving a particular dose that would be unable to perform any task at a series of times from 1 minute to 24 days postdetonation.

Figures 4-1 to 4-3 show 25, 50 and 75 percent performance curves versus time. These curves show what doses would be required to cause 25, 50 or 75 percent of enemy troops to be incapacitated. For example, if it is assumed that the loss of 50 percent of a force completely inactivates is, then one could examine Figure 4-1 for physically undemanding tasks at N/g = 4:10 and interpret it as follows: irradiating an opposing force with 3500 cGy would knock out 50 percent within four minutes, but by 12 minutes many would recover. In order to incapacitate 50 percent of a force permanently, the average radiation dose to the force must exceed 7400 cGy.

The example above only includes the effect of ETI produced by high doses of radiation within the first several hours after exposure. The use of these data are best limited to two hours postirradiation because after that time, the other physiological effects, caused by much lower doses, of ionizing radiation dominate.

The Intermediate Dose Panel, convened by the Defense Nuclear Agency has done extensive studies in which effects of intermediate doses (50 to 4500 cGy) on task performances (Anno, 1984) were estimated.

Figures 4-4 and 4-5 from the IDP study show 10, 25 and 50 percent incapacitation curves for physically undemanding (VDT) tasks superimposed on 10 to 90 percent isoperformance curves, developed by the IDP. These curves show that, up to 1 hour after irradiation, the incapacitation dominates, but that within five hours, performance is degraded to <20 percent of pre-injury levels at 3000 cGy.

If it were necessary to reduce the combat effectiveness of an attacking enemy force to a combat ineffective state within two hours, then the higher doses that produce incapacitation are called for. If the time is less critical, for instance, in preparation for an attack by our forces, then much lower doses can achieve the same objectives and cover a larger area.

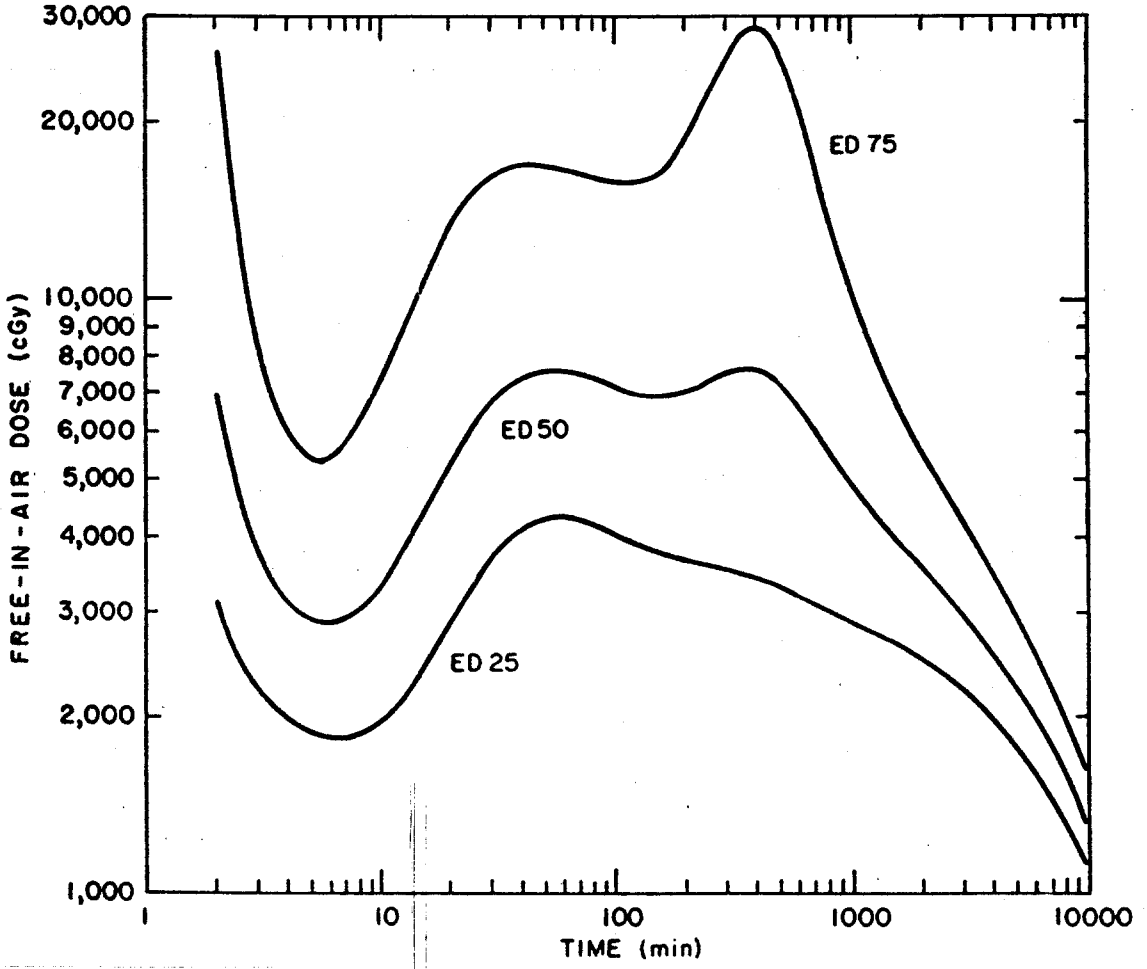


Figure 4-1. Doses that produce 25, 50 and 75 percent incapacitated versus time for VDT N/g=4:10 field.

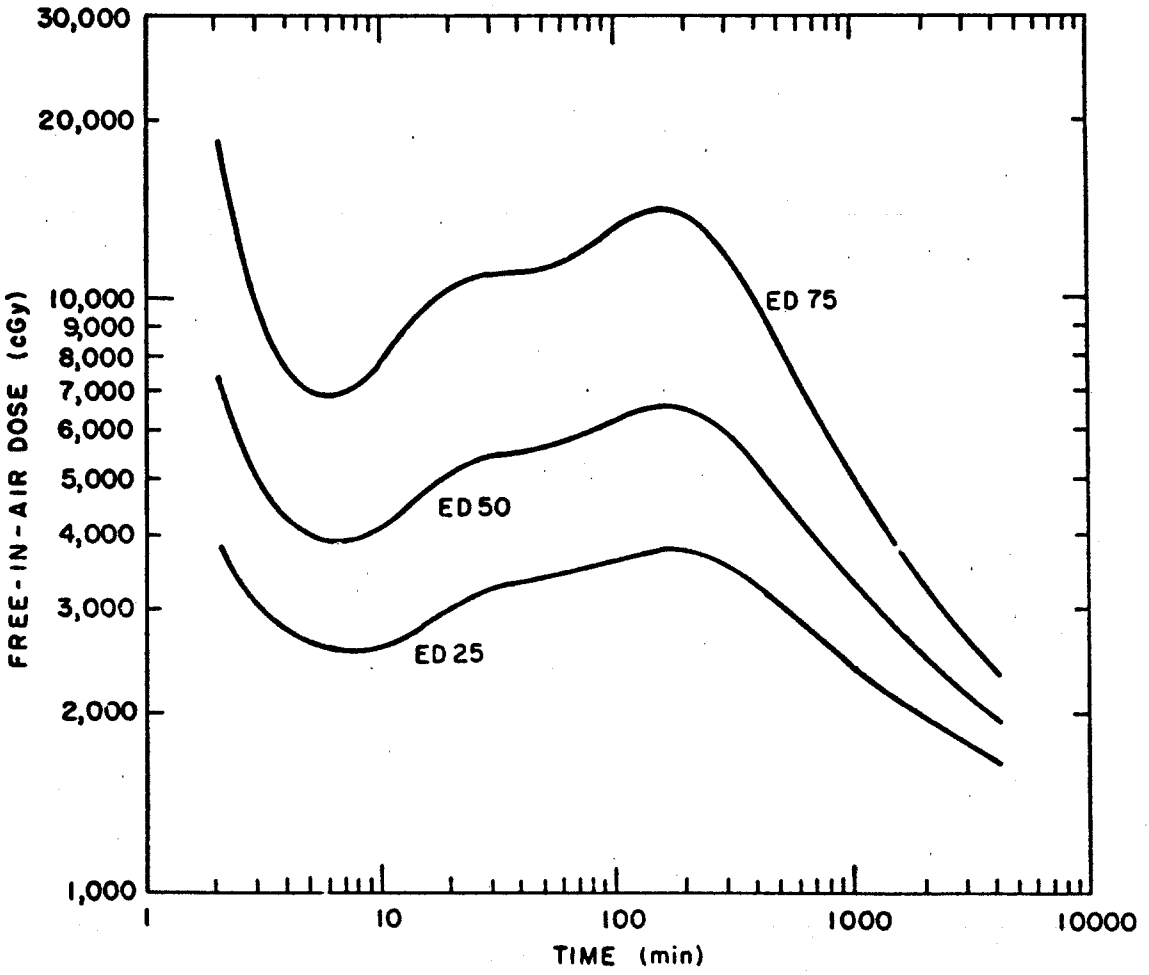


Figure 4-2. Doses that produce 25, 50 and 75 percent incapacitated versus time for VDT N/g=3:1 field.

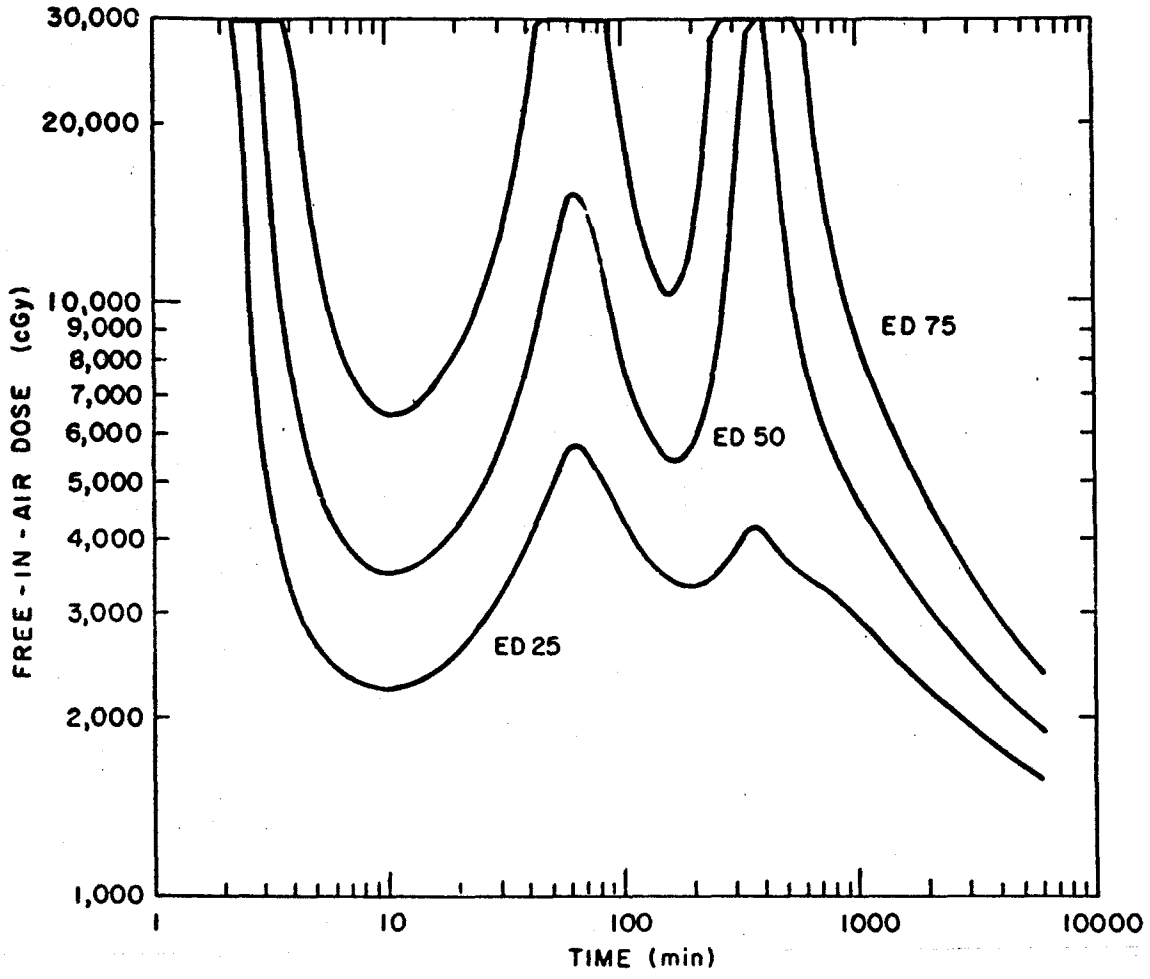


Figure 4-3. Doses that produce 25, 50 and 75 percent incapacitated versus time for PAW tasks N/g=3:1, field.

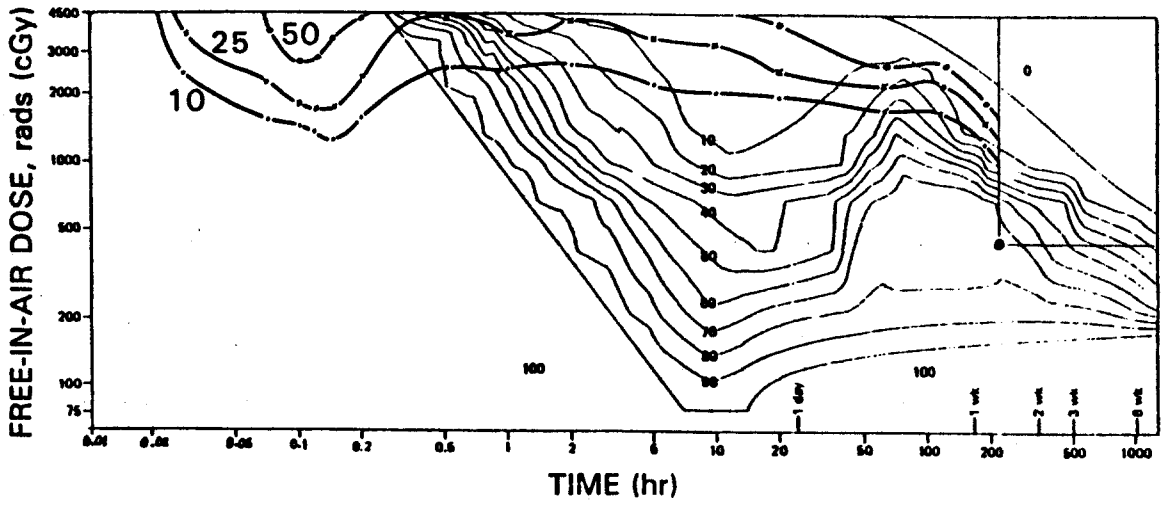


Figure 4-4. 10, 25 and 50 percent incapacitated curves superimposed on 10-90 percent performance degradation curves for physically undemanding tasks N/g=4:10 field.

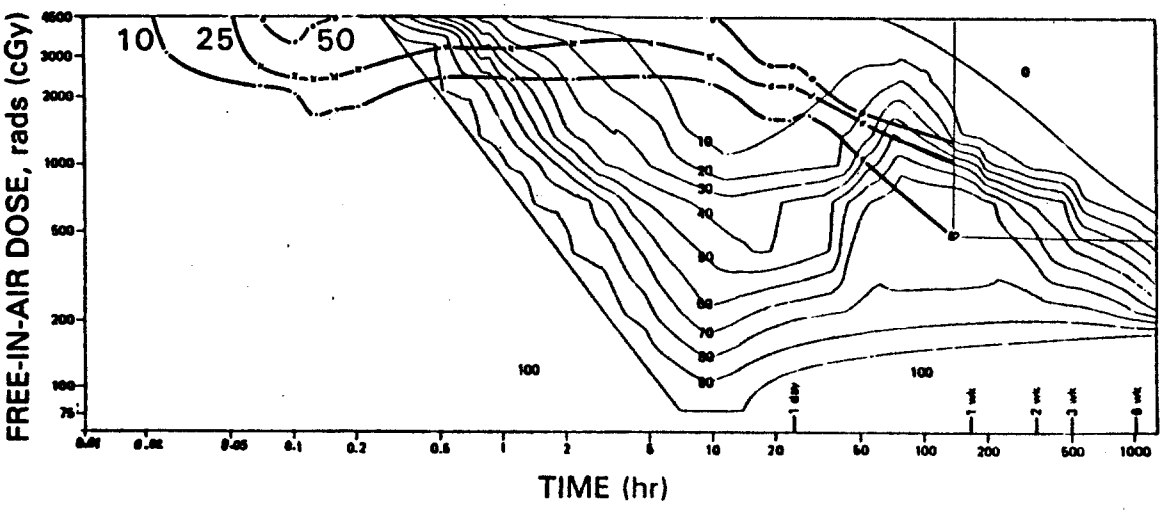


Figure 4-5. 10, 25 and 50 percent incapacitated curves superimposed on 10-90 percent performance degradation curves for physically undemanding tasks N/g=3:1 field.

SECTION 5

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APPENDIX

DEVELOPMENT OF A METHOD TO GENERATE TIME HISTORIES

A.1 TIME DEPENDENT BEHAVIOR.

The individual minute-by-minute probit lines can be used to predict the percent incapacitated versus time at any particular dose. The percent incapacitated is an expected value that describes the average percentage of individuals not performing at any given time. However, these expected values do not describe the behavior of individuals or groups over time. The individual behaviors over time can be described generally as alternating periods of performance and nonperformance after receiving a dose of radiation. Group behavior can be described by the average of a large number of the individual behaviors. In the ensemble it must be true that the average number incapacitated at any time is consistent with that predicted by the probit line for that dose. Since a number of combat models make use of individual behavior, it is necessary to provide a method (model) to generate as many individual time histories as required in their Monte Carlo calculation.

Since the amount of animal data available at or near any dose was limited, construction of a model required a number of assumptions. A typical life history of an animal is depicted in Figure A.1. At time zero, the animal is assumed to have received some dose of radiation. What ensues is a series of periods of performance (up) and nonperformance (down). There can be as many as k down periods, where k may be and often is zero (depending on dose). The doses given these animals are superlethal, hence all animals eventually reach a state of PCI. PCI may occur at any time, but is generally later for lower radiation dose. The number of down periods, k, is arbitrary, and the general model will be described specifically later.

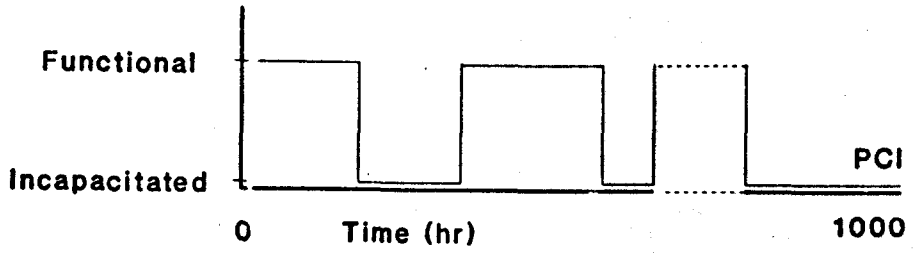


Figure A.1. Typical life history of an irradiated animal illustrating periods during which the subject is functional (up) and periods when the subject is non-functional (down).

Ignoring PCI (to be considered later), a model performance history can be made by assuming that the length of an up or down period is a random variable with distribution (density) f_i, i.e.,

(up, down) distributed as f_i ($\underline{\alpha}_i$,t),

where,

i=1,2,...,2k
$\underline{\alpha}_i$ = a vector of parameters of the distribution, not containing dose
t = the length of the interval

For k down periods there are 2k intervals. The f_i are assumed to be independent and defined on the interval (o, ∞). This means that the length of any up or down period does not depend on the length of any other period.

The actual time (measured from zero) that an interval ends (begins) is obtained by adding together the lengths of intervals to that point. The distribution of that point must therefore be described by convolution. The convolution of distributions of interval lengths from 1 to j, is

$$f_{12...j} = f_1 * f_2 *...*f_j$$

where $f_{12...j}$ is the distribution of the sum of j intervals whose individual distributions are f_1, f_2, ..., f_j and * means convolution.

Now let $P_k(T)$ be the probability that an individual is not incapacitated at time $T \geq 0$. Time T is the time after receiving some dose of radiation (see Figure A-1). Let $P_k(T)$ be the probability that an individual is not incapacitated at time $T \geq 0$. Then

for $k \geq 2$

$$P_k(T) = \int_T^\infty f_1(\underline{\alpha}_1, t)dt + \sum_{i=1}^{k-i} \int_o^T \int_{T-x}^\infty f_{1\ldots 2i}(\underline{a}, x) f_{2i+1}(\underline{\alpha}_{2i+1}, t)dtdx +$$

$$\int_o^T f_{1\ldots 2k}(\underline{b}, t)dt$$

for $k = 1$

$$P_k(T) = \int_T^\infty f_1(\underline{\alpha}_1, t)dt + \int_o^T f_{12}(\underline{b}, t)dt$$

The terms in $P_k(T)$ are probabilities that T falls in an up period. The first term is the probability that T falls in the first up period, and the last term is the probability that T falls in the last up period. For $k \geq 2$ (two or more periods), the middle terms in the summation are the probabilities that T falls in the intervening up periods. For $k = 1$, these intervening periods do not exist, and there are only the first and last terms. For $k = 0$, $P_o(T)$ is defined to be 1 for all T. The vectors $\underline{a}$, $\underline{b}$ in the convolution distributions are parameters for these distributions; subscript notation on these parameters was dropped for lack of space.

PCI is added by assuming that time to PCI has some distribution, h. If TD is a random variable expressing time to PCI, then

TD distributed as $h(\underline{\alpha}, t)$

The probability that an individual is up at some time T can now be expressed with PCI included. This probability is

$$\left(\int_T^\infty h(\underline{\alpha}, t)dt\right) P_k(T) \qquad \text{(A.1)}$$

This expression says that an individual is up at time T if he has not reached PCI and is not experiencing other incapacitation.

To complete the model for life histories, another set of probabilities must be introduced. An individual can experience anywhere from zero to k down periods. Let PE_i represent the probability that, at most, i down periods occur (i=o, ..., k), and where $\Sigma PE_i=1$. The exact values these probabilities take will in general depend on dose. For instance, PE_o (the probability of no down periods) will be smaller for higher doses of radiation and larger for smaller doses of radiation. For a particular dose, the number of down periods is not observed to be related to time to PCI, and therefore the probabilities PE are assumed independent of this factor.

Using these probabilities, the expression for the probability of being up at time T takes the form

$$PU_k(T) = \int_T^\infty h(\underline{\alpha},t)dt \sum_{i=0}^{k} PE_i P_i(T) \qquad (A.2)$$

This probability differs from equation A.1 in that is not confined to the case of life histories with k down periods, but covers the more realistic situation that life histories will vary in number of down periods, with a frequency related to the probabilities PE.

If $PU_k(T)$ is the probability of being up at time T, then 1 minus $PU_k(T)$ is the probability of being down at time T, and is called $PD_k(T)$. Thus

$$PD_k(T) = 1 - PU_k(T)$$

The subscript k on PD_k in this case indicates the maximum number of down periods possible.

It is now possible to relate PD_k to the minute-by-minute incapacitation curves generated from the fitted probit lines. If $PD_k(T)$ is given a frequency interpretation, then $PD_k(T)$ represents an expected fraction (or percent when multiplied by 100) incapacitated at time T. Thus PD_k and the minute-by-minute incapacitation curves can be looked at as representing the same quantities. The minute-by-minute incapacitation curves are summaries of aggregate behavior in terms of proportion incapacitated, and PD_k relates this proportion incapacitated to the probabilistic distributions associated with individual behavior. The idea, then, is for a choice of these distributions to make $PD_k(T)$ take the values, as nearly as possible, of the minute-by-minute incapacitation curves. For a particular minute-by-minute curve of incapacitation versus time (associated with a specific radiation dose), this becomes a fitting problem. A least squares fit of $PD_k(T)$ to a minute-by-minute curve would give values of the parameters for the distributions of time to PCI and lengths of up and down periods associated with individual behavior. These distributions could then be used to generate life histories of individuals, using Monte Carlo techniques, described later. This is what was desired; and to the extent that $PD_k(T)$ is a good fit to the minute-by-minute curve, that curve will be said to have been decomposed.

A.2 PROBABILITY DISTRIBUTIONS.

At this point, a discussion and justification for aspects of the decomposition of the data in this report are made. A description is given of the actual distributions used in the decomposition along with the resulting expressions for $P_k(T)$ and $PD_k(T)$. The distribution of interval lengths was assumed to be exponential, i.e.,

$$f_i(\underline{\alpha}_i,t) = (1/T_i)\exp(-t/T_i), \qquad t\geq 0$$

This exponential distribution has mean T_i and variance T_i'. The exponential distribution is defined on the nonnegative real line and thus does not allow negative interval lengths, a restriction mentioned earlier. To further support the use of this distribution, the cumulative histograms (empirical distribution) for time to the first down period and the length of the first down period were tabulated for the visual discrimination task. Since there were only 15 observations in the N/g = 3:1 data, these data were combined with those for N/g = 4:10. The data were then combined across doses. This could be done since the correlation between dose and time-to-first-down-period and dose and length-of-first-down-period were negligible. This provided approximately 75 data points in the empirical distribution which are plotted in Figures A.2 and A.3. Plotted also (as the smooth curves) are the fitted exponential distribution functions with parameters of 3.25 minutes for the time to the first down period and 14.25 minutes for the length of the first down period. The empirical distribution S(x) has a value that is the proportion of intervals less than or equal to x minutes in length. As Figures A.2 and A.3 indicate, the agreement between the empirical distributions and the exponential functions is quite good. The Kolmogorov Goodness-of-Fit Test does not reject the exponential distribution in either case for α=.01.

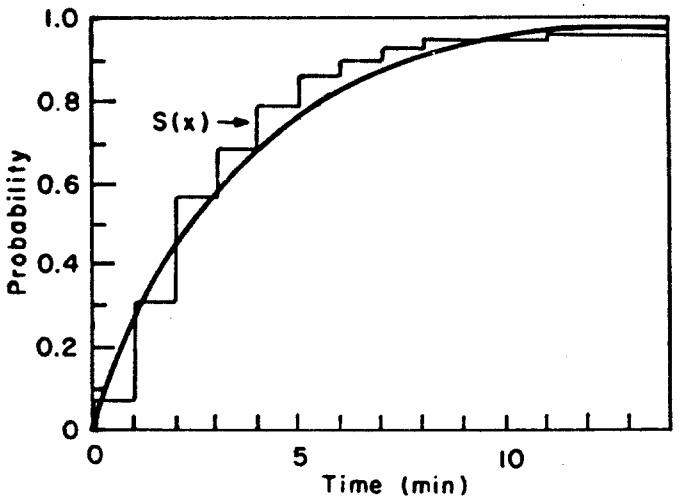


Figure A.2. Time to first down period. S(x) is the empirical distribution.

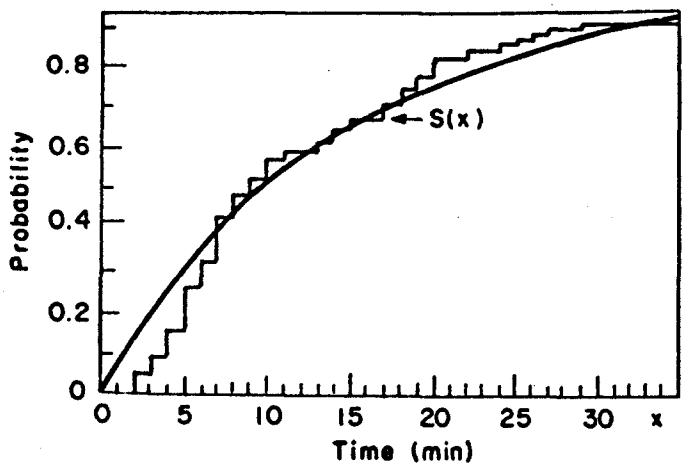


Figure A.3. Length of first down period. S(x) is the empirical distribution.

The distributions of other intervals were assumed to be exponential also but could not be tested because of the small number of data points available.

The distribution of time to PCI, h, was assumed to be a Weibull distribution, i.e.,

$$h(\underline{\alpha},t) = \alpha\beta t^{\beta-1}\exp(-\alpha t^{\beta}),\ t\geq 0$$

This distribution is also defined on the nonnegative real line, and therefore does not allow for negative time to PCI. It should be emphasized that this distribution does not represent the time to final incapacitation for every individual. In the process of generating life histories, individuals may experience incapacitation before PCI. If the individual does not recover, an early termination of performance is brought about. This early termination of performance can be viewed as "early PCI", occurring during a down period. In this way, the Weibull distribution is being used to help model these early ends of performance. This type of phenomenon will be mentioned again in the next section.

A.3 FUNCTIONAL FORM OF DECOMPOSITION.

From the specific distributions, the resulting expressions for $P_k(T)$ and $PD_k(T)$ are given by

$$PD_k(T)=1-\exp(-\alpha T^{\beta})\sum_{i=0}^{k} PE_i P_i(T)$$

where for $m\geq 2$

$$P_m(T)= \exp(-T/T_i)+$$

$$\sum_{i=1}^{m-1}\exp(-T/T_{2i+1})\sum_{j=1}^{2i}\frac{A_j T_{2i+1}}{T_{2i+1}-T_j}(1-\exp[-T(T_{2i+1}-T_j)/(T_j T_{2i+1})])+$$

$$\sum_{j=1}^{2m} A_j[(1-\exp(-T/T_j)] \qquad A_j=T_j^{2i-1}\sum_{\substack{\tau=1\\ \tau\neq j}}^{2i}\frac{1}{T_j-T_\tau}$$

for $m=1$

$$P_1(T)=\exp(-T/T_1)+\sum_{j=1}^{2} A_j[(1-\exp(-T/T_j)] \qquad A_j=T_j\prod_{\substack{\tau=1\\ \tau\neq j}}^{2}\frac{1}{T_j-T_\tau}$$

and for $m=0$, we defined, $P_o(T) = 1$ for all $T \geq 0$

When actually fitting PD_k to minute-by-minute probit curves for the visual discrimination task, the maximum number of down periods, k, was assumed to be three. This was observed to be approximately true since only two animals had more down periods than this. Most VDT animals experienced only one transient down period which generally began within 10 minutes after irradiation. Occurrences of two and three down periods were generally observed among animals receiving higher doses.

The performance of animals on the physical activity wheel (PAW) exhibited a different up-down pattern than that for animals performing the visual discrimination task. Approximately half of

the PAW animals had more than three down periods, and a few had as many as 14 down periods before PCI. A decision to model life histories for PAW animals using a maximum of 9 possible down periods (i.e., k=0, 1,...,9) was made due to limitations on computing time and because the inclusion of additional down periods would not appreciably improve the fit of PD to the data. The assumption that the distributions of the length of down periods and up periods were independent of k (the number of down periods) was adequately supported by the data and resulted in a model with a total of 18 parameters to be fitted.

A.4 FITTING THE FUNCTION PD_3.

The use of Monte Carlo techniques to construct life histories like those in Figure A.1 is best demonstrated with an example. The use and explanation of the coefficients in Tables A.1 through A.3 are also made with reference to the fit to a particular curve. The fit of $PD_3(T)$ to the 3000 cGy FIA (N/g = 4:10) curve for VDT animals is used for this purpose and is shown later as the smooth curve in Figures A.7 through A.9.

A.4.1 Determination of Probability of the Number of Down Periods.

In each fit of PD_3 to the minute-by-minute probit curves, the parameters (probabilities) PE were not computed. These parameters were treated as constants in the fitting process, and were assigned values obtained from other considerations before the fit was made. The values for these parameters were different for each curve. For the visual discrimination task, their values depended on the incapacitation activity during the first 2 hours. For this reason, PE_0 was assigned a value very near the probability of not having an incapacitation during that period. The other PE values were assigned considering the observation that a larger number of down periods tended to occur for higher doses. In general, PE_3 would, for instance, be made larger for larger doses. Figure A.4 shows a probit line (a)fitted to the data where incapacitation

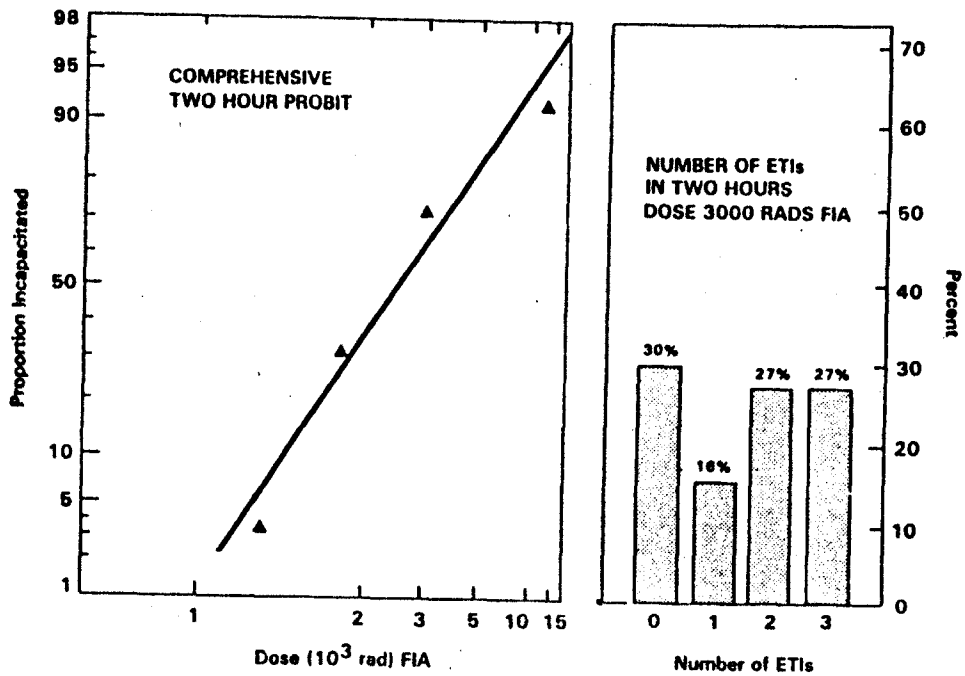
is defined as any incapacitation in the first 2 hours. The fitted probit line indicates that for 3000 cGy FIA, the percent incapacitated is about 65%; i.e., $1-PE_0$ is about 65%. Allowing for a few percent additional incapacitation after two hours, this puts PE_0 = 28%, which was its assigned value. After the value for PE_0 was determined, the values for the other PE's were assigned using the same considerations and the fact that the PE's must sum to 100%. The values assigned for the 3000 cGy curve appear in Figure A.4.

Like the VDT animals, the PAW animals showed a tendency for more down periods to occur for larger doses and for PE_0 to decrease as doses increase. Since a larger number of PE values were involved for the PAW animals, a functional form that depended on dose was used for their generation. For this purpose, two truncated geometric distributions were used. One of these distributions (f_L) was used to approximate the probability of having down periods for low doses, while the other (f_H) was used to approximate the probability of down periods for high doses. These two distributions were used to form a mixture distribution that was a function of dose. If P (not to be confused with P_k) represents this mixture distribution and D represents dose, then

P is defined as

$$P(D,k) = p(D)f_L(k) + (1 - p(D))\ f_H(k)$$

where k = 0, 1, 2, ..., 9 and $0 \leq p(D) \leq 1$. p was a linear function of dose that decreased from a maximum value at a low dose of 1500 cGy to a minimum value at a high dose of 8000 cGy. This was the span of doses encompassed in Table A.3 and by the PAW animals. The mixture distribution P was used to generate the values of PE_k for each dose, $1500 \leq D \leq 8000$, and for each k, $PE_k = P(D,k)$. These values appear at the bottom of Table A.3. The PE values for the VDT animals appear in Tables A.1 and A.2.



(a) Comprehensive 2-hour probit

(b) Percent of down peri
for 3000 cGy FIA dos

Figure A.4. Graphs for parameter estimation for VDT, N/g = 4:1
field.

Table A.1. Coefficients for visual discrimination task, N/g=4:10.

FIA Dose (cGy)		1000	1500	2000	2500	3000	5000	8000	15000
One Down Period	T_1	(No Early Incapacitation)	1.681	2.504	2.073	2.237	1.233	1.3	.967
	T_2		14.008	10.617	14.566	12.86	51.946	19.414	27.824
Two Down Periods	T_3		1.672	2.503	2.069	1.811	1.014	.701	.458
	T_4		14.58	10.801	14.9	3×10^5	.448	.181	.304
	T_5		509.594	327.089	246.84	.06	.848	.689	.503
	T_6		1217.049	13761.6	3×10^5	3×10^5	13.753	299.472	3×10^5
Three Down Periods	T_7		1.556	2.32	1.97	2.063	1.408	1.265	0.953
	T_8		6.169	5.127	5.976	6.729	20.651	22.362	31.252
	T_9		.06	.06	.06	.06	41.617	54.964	31.861
	T_{10}		6.063	5.104	5.893	6.639	333.321	361.718	120.772
	T_{11}		3×10^5	77.149	71.664	36.608	1930.232	417.788	.06
	T_{12}		.06	17799.000	3×10^5	1817.814	35318.072	7244.976	120.251
Dist of PCI	α	2.662×10^{-28}	6.641×10^{-13}	2.347×10^{-13}	9.1564×10^{-9}	3.6117×10^{-4}	4.891×10^{-3}	5.412×10^{-4}	5.192×10^{-4}
	β	6.6309	2.943596	3.1062	2.1534	.9895	.70911	1.06	1.1322
Time Shift (min)		2.0	1.8	1.5	1.2	1.0	.9	.75	.75

	Probabilities of k Possible Incapacitations (PE)							
k								
0	1.0	.82	.5	.42	.28	.15	.05	.01
1	0.0	.10	.38	.41	.65	.25	.2	.22
2	0.0	.06	.1	.10	.04	.3	.35	37
3	0.0	.02	.02	.07	.03	.3	.40	.4

Table A.2. Coefficients for visual discrimination task, N/g=3:1.

FIA Dose (cGy)		1000	1500	2000	2500	3000	5000	8000	15000
One Down Period	T_1	(No Early Incapacitation)	3.625	2.737	2.432	2.338	1.444	1.164	.844
	T_2		15.328	136.126	139.64	101.516	194.089	307.474	3×10^5
Two Down Periods	T_3		3.42	3.136	3.074	2.819	1.468	1.166	.905
	T_4		3.898	20.442	8.204	10.176	79.732	82.014	175.585
	T_5		.499	58.106	896.189	75.127	20.662	.06	17.566
	T_6		4.405	119.046	4136.432	151.691	094.58	3.268	13.226
Three Down Periods	T_7		3.423	2.987	2.707	2.545	1.588	1.319	1.053
	T_8		3.926	7.342	4.545	4.360	4.849	5.58	8.197
	T_9		.496	.06	.177	.144	.06	.06	.06
	T_{10}		4.421	7.303	4.579	4.394	4.743	5.345	5.905
	T_{11}		4649.753	41,102.76	866.386	7854.102	806.918	22.21	14.915
	T_{12}		25775.76	3×10^5	3829.072	3×10^5	5723.356	2036.58	55.802
Dist of PCI	α	3.309×10^{-13}	1.665×10^{-9}	3.388×10^{-5}	1.608×10^{-5}	1.786×10^{-4}	1.192×10^{-3}	2.4×10^{-3}	1.047×10^{-2}
	β	3.10511	2.269	1.2146	1.3991	1.1705	1.017	.9935	.8328
Time Shift (min)		2.0	2.0	1.0	1.0	1.0	.85	.8	.6

Probabilities of k Possible Incapacitations (PE)

k							
0	1.0	.92	.82	.67	.52	.3	.15	.05
1	0.0	.02	.03	.15	.2	.3	.25	.3
2	0.0	.04	.05	.09	.14	.2	.4	.4
3	0.0	.02	.1	.09	.14	.2	.2	.25

Table A.3. Physical activity wheel coefficients, N/g=3:1.

FIA Dose (cGy)		1000	1500	2000	2500	3000	5000	8000
Down Periods								
	T_1		22.602	10.020	10.074	4.140	3.000	3.360
1	T_2		3.000	5.220	10.200	7.380	13.800	12.360
	T_3		98.520	71.940	120.000	5.040	4.080	4.200
2	T_4		3.180	3.180	3.000	3.060	5.580	5.220
	T_5		61.620	69.060	68.280	7.380	5.580	6.120
3	T_6		3.120	3.120	20.520	5.220	6.960	7.980
	T_7		51.540	80.520	9.440	118.620	49.080	40.560
4	T_8		3.240	3.000	6.000	13.200	3.840	3.780
	T_9		41.940	73.620	55.620	18.000	29.220	33.720
5	T_{10}		3.300	28.200	15.600	28.200	28.140	28.200
	T_{11}		34.620	24.720	19.260	120.000	3.240	3.240
6	T_{12}		28.200	28.140	25.980	3.240	28.200	28.140
	T_{13}		5.580	3.240	9.000	57.300	5.340	4.500
7	T_{14}		28.140	28.200	27.540	28.140	23.220	28.200
	T_{15}		3.180	3.000	12.000	15.900	3.060	3.120
8	T_{16}		28.200	28.140	24.840	28.140	16.200	28.200
	T_{17}		3.300	3.000	3.000	3.000	3.900	3.720
9	T_{18}		28.200	28.020	20.760	28.140	7.020	6.240
Dist of	α	3.309×10^{-13}	7.492×10^{-10}	1.031×10^{-5}	1.13×10^{-4}	6.39×10^{-4}	9.568×10^{-4}	9.729×10^{-6}
PCI	β	3.10511	2.29099	1.313625	1.08627	.91506	.9828	1.69671
Time Shift (min)		2.00000	2.00000	2.000000	2.00000	2.00000	2.0000	2.00000
				Probabilities of k Possible Incapacitations (PE)				
k								
0		1.000	.3041	.2720	.2397	.2075	.0786	.0028
1		0.000	.1790	.1604	.1418	.1233	.0490	.0048
2		0.000	.1064	.0961	.0857	.0754	.0339	.0083
3		0.000	.0653	.0601	.0547	.0497	.0290	.0144
4		0.000	.0433	.0417	.0403	.0386	.0322	.0252
5		0.000	.0341	.0357	.0372	.0388	.0451	.0441
6		0.000	.0349	.0401	.0453	.0505	.0713	.0776
7		0.000	.0460	.0564	.0667	.0771	.1185	.1374
8		0.000	.0707	.0892	.1078	.1263	.2006	.2450
9		0.000	.1162	.1483	.1806	.2128	.3418	.4404

A.4.2 Iterative Adjustment of Parameters.

Fitting PD_3 for assigned values of the PE probabilities was done by the Least Squares method. Because PD_3 is a complicated function, a nongradient routine (STEPIT) was used to calculate this fit. The fit was made to minute-by-minute probit values that were used in creating the curves in figures 10 and 11. With the probabilities PE fixed, the process involves iteratively adjusting the 14 remaining parameters (T_1, ..., T_{12}, α, β) until a least squares solution is obtained. Two of these parameters are associated with P_1 for the distribution of time to the first down period and the length of the first down period. Four more parameters are associated with P_2 in a similar way for the two down periods in this case. There are six parameters for the case of P_3, and in general, 2k parameters for P_k. Two parameters (α, β) are left, and they are for the distribution of time to PCI. This accounts for all parameters, and these are the first 14 listed in Tables A.1 and A.2.

A slight change was made for the fit to the 1000-cGy curve for both the PAW and VDT data. Here PE_o was assumed 1, and therefore all other PE values were 0. In other words, the 1000-cGy curve does not assume any incapacitation except PCI. Tables A.1 through A.3 reflect this by showing values only for parameters α, β, and PE for the 1000 cGy curve. This assumption was entirely justified, since very few early incapacitations are observed at this dose.

A.5 MONTE CARLO TIME HISTORY GENERATION.

After a fit has been made, the 14 parameters can be used in a Monte Carlo technique to generate life histories consistent with the fitted curve. A life history of the 3000 cGy curve will be generated to illustrate the method and to further explain Tables

A.1 through A.3 and the use of the coefficients. The Monte Carlo technique uses random numbers (RN) uniformly generated on the interval (0, 1) and the associated distributions in the fit of PD_3. The first random number generated is used to select the number of down periods possible in the life history. If this random number is between 0 and .28 then (Table A.1) for the 3000 cGy curve K=0 and, a life history with no incapacitation before PCI is selected. If the random number is between .28 and .93 (.28 + .65), a life history with one possible down period is selected. If the number is between .93 and .97 (.93 + .04), a life history with two possible down periods is selected. If the number is greater than .97, a life history with three possible down periods is selected. This process generates life histories where the number of down periods occurs with a frequency related to the values of PE. Assume that the first random number generated is .2841. A life history with one possible down period is then selected. This means that the first two coefficients (T_1, T_2) in Table A.1 under 3000 cGy are now used. Another random number is generated and used to select the time T1 to the first down period using that exponential distribution function. In general, a random interval from an exponential distribution is given by $-T_i[\ln(RN)]$ for a given random number RN and coefficient T_i. "ln" here refers to the natural logarithm. If this random number RN = .2009, then in this case, using the first coefficient from Table A.1 yields

$$T1 = -2.237 \ln (.2009) = 3.59 \text{ minutes}$$

The shift parameter of 1 minute is added to this number, and the time to the first down period is 4.59 minutes. The shift parameter is in the tables just above the PE coefficients, and is added because the fitting of PD_3 for the 3000 cGy curve was done with time shifted 1 minute. This shift was made because the minute-by-minute probit curve for 3000 cGy goes to zero near 1

minute. The shift adjusts the time of zero incapacitation for the minute-by-minute probit curve to agree with that for fitted time. It is a small adjustment, and is added to the time to the first down period and to the time to PCI for every life history. Figure A.5 further illustrates how times like 3.59 minutes are obtained. Figure A.5 is a plot of the distribution function for f_1, the density function of time to the first down period (less the shift). RN is a probability value on the ordinate (Y axis), and T1 is simply the associated value on the abscissa (X axis) obtained by using the plotted curve. To obtain the duration of the first down period T2, another random number RN is generated, and the second parameter (12.86) from Table A.1 is used. If RN is .63156 in this case, then T2 = -12.86 ln (.63156) = 5.91 min.

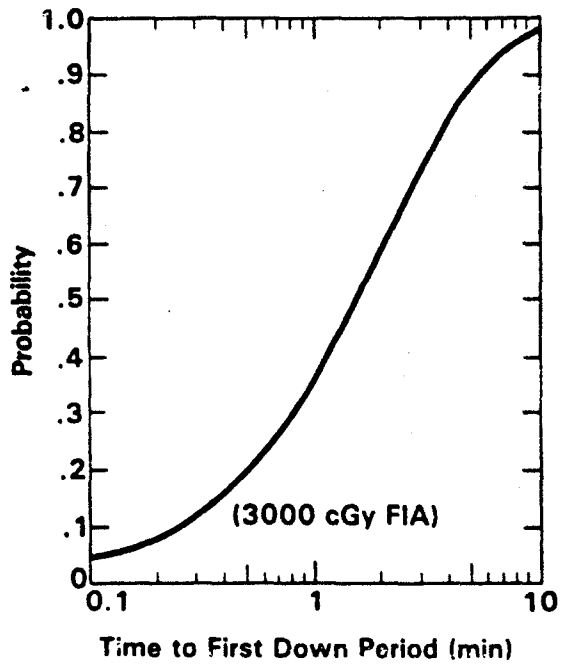


Figure A.5. Distribution function of time to first down period.

To obtain the time for the end of the first down period, 4.59 minutes is added to 72 minutes to give 10.5 minutes. Time to PCI now is the only thing needed to complete this life history. Time

to PCI has a Weibull distribution, and the parameters α and β in the table must be used. These parameters (3.6117×10^{-4} and .9895) are used in the Weibull distribution function to generate a time to PCI, TD. Another random number RN is used for this purpose. In general, a random interval TD from the Weibull distribution is generated using the formula

$$\log TD = (1/\beta) \log [(-\ln RN)/\alpha]$$

for a given α, β, and where log is the logarithm to the base 10. Assume RN this time to be .3963; then TD is obtained as follows:

$$\log TD = (1/.9895) \log [-\ln(.3963)/3.6117 \times 10^{-4}]$$

$$TD = 10^{\log TD} = 2786 \text{ minutes}$$

The shift of 1 minute is added to this number to give TD = 2787 minutes. This then completes the generation of the life history, which consists of an individual who is incapacitated from 4.59 minutes to 10.5 minutes and has a PCI at 2787 minutes. If the random number used to select the number of possible down periods had dictated more than one possible down period, the above process would have continued to generate the necessary up and down intervals and times using the coefficients in the Table for the number of down periods in the life history. The coefficients in the Tables for each number of down periods alternate between applying first to an up period and then to a down period and then to an up period, etc., depending on the number of periods selected. Generating life histories for the PAW data proceeds somewhat differently. The coefficients are in Table A.3. In this case, the coefficients for a distribution are chosen independently of k (the number of down periods). For instance, for a life history with one down period (k = 1 for some dose), the same first two coefficients in Table A.3 would be used as

for a life history with more than one down period (k>1 for the same dose). For this reason the coefficients in Table A.3 are not segregated by k as they are in Tables A.1 and A.2, but are otherwise listed in the same way alternately for up periods and then down periods. The generation of life histories for the PAW data is otherwise the same as that for VDT.

Two other items remain to be discussed concerning the generation of life histories. Since time to PCI is generated separately from other incapacitation, it can terminate a life history at any point. If PCI occurs during a down period, for instance, the beginning of that period then becomes the effective time to beginning of PCI. In this way the effective time to PCI can be altered to account for "early" PCI. If PCI occurs between two down periods, the last down period is lost. The second item concerns rounding the intervals of time. If a generated interval of time is less than 30 seconds in length, it is rounded to 0. If it is between 30 seconds and 1 minute in length, it is rounded to 1 minute. This is done to adhere to the basic definition of incapacitation. It also avoids having to deal with intervals of infinitesimal length, and ensures that all intervals are at least 1 minute long.

PCI and rounding can in practice alter the actual frequencies of down periods generated from that indicated by the PE coefficients. This is the reason for use of the terminology "possible down period(s)". In the fitting of PD to a minute-by-minute curve, the frequency of one, two, and three down periods is dictated generally by the shape of that curve. Curves that indicate periods of secondary incapacitation will naturally require two and three down periods. The coefficients of a fitted curve, along with its shape, are the best indicators of the actual frequency of down periods likely to be generated.

A.6 MONTE CARLO GENERATED HISTORIES.

In Figure A.6 are ten life histories. The heavy lines indicate periods of incapacitation, and the dashed lines indicate periods when the individual is up. The first life history in this Figure is the one generated in the example above. The other histories were generated the same way. This type of Monte Carlo generation of life histories was done for 10, 100 and 1000 such iterations, and the fraction of the life histories that produced incapacitation at various times was observed. These fractions are plotted in Figures A.7 through A.9 using the solid triangle symbols. The smooth heavy curve in these Figures is a plot of the fitted PD_3 and the minute-by-minute probit is shown with a thin line.

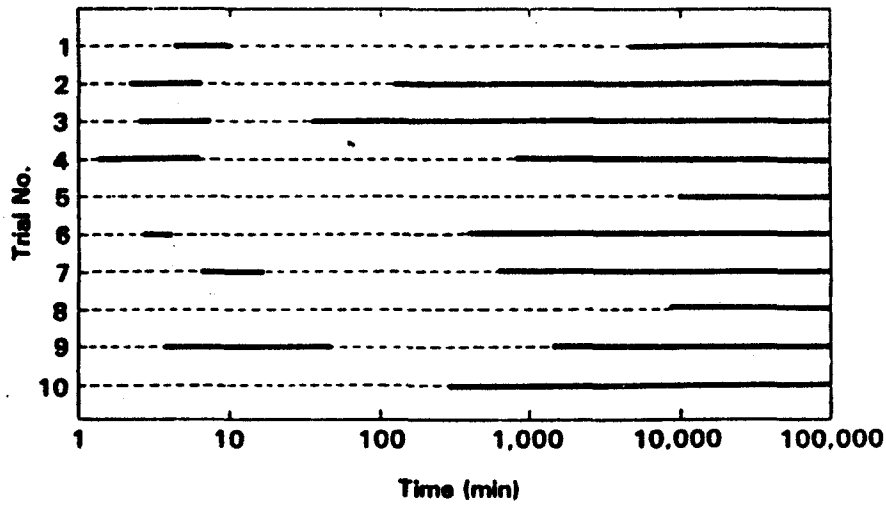


Figure A.6. Monte Carlo life histories for N/g = 4:10 Yield 3000 cGy FIA

Figures A.7 through A.9 illustrate that the calculated PD_3 values at each time become progressively closer to the probit values as the number of iterations increases. The plot of PD_3 also shows

that it is a high contact representation of the probit curves. The Monte Carlo technique, then, is a way to generate life histories representative of these data. The coefficients in Tables A.1 through A.3 are provided for use in models employing the Monte Carlo technique.

The fits of PD_k to the minute-by-minute probit curves also served as a method of smocthing the data for both the visual discrimination task and PAW data. These smoothed curves were made using the coefficients in Tables A.1 through A.3 and appear in Figures 3-10, 3-11 and 3-15.

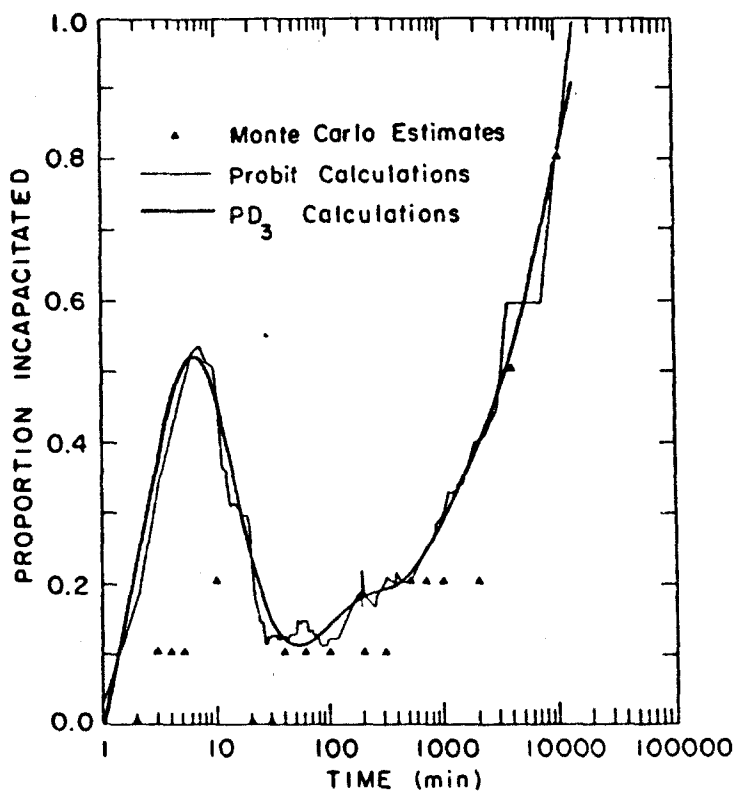


Figure A.7. Ten Monte Carlo iterations 3000 cGy FIA N/g = 4:10 field.

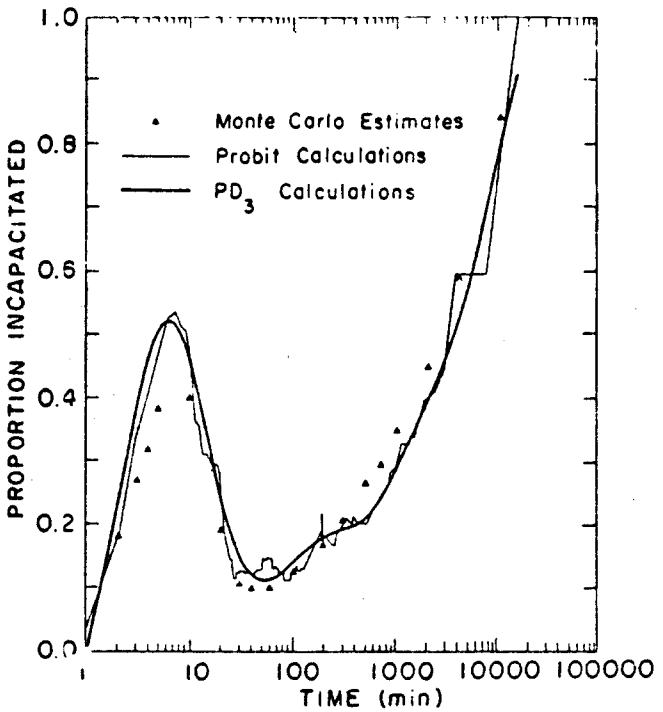


Figure A.8. One hundred Monte Carlo iterations 3000 cGy FIA N/g = 4:10 field.

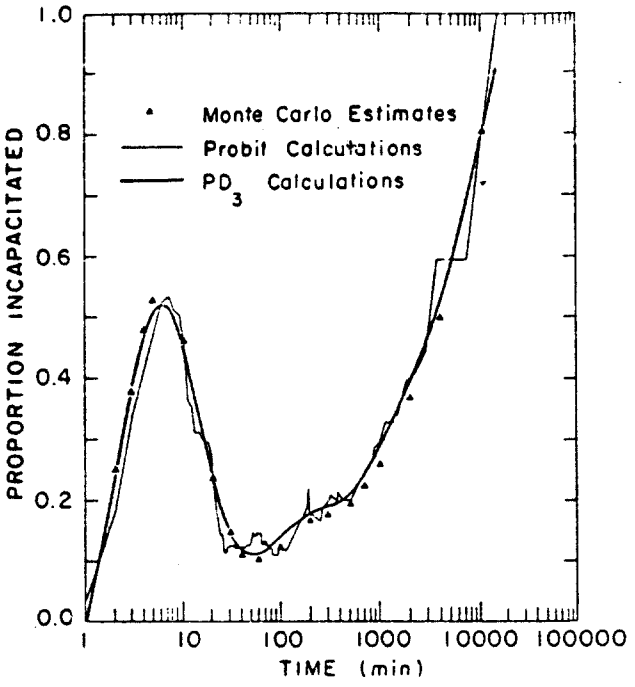


Figure A.9. One thousand Monte Carlo iterations 3000 cGy FIA N/g = 4:10 field.

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